A million and 1

A poetic understatement

The actual number is in the billions. For more than 15 years, Dalmane (flurazepam HCl/Roche) has been providing sleep that satisfies patients—sleep that comes quickly and lasts through the night.[1-8]

Sleep that satisfies *you*—you can count on an exceptionally wide margin of safety.[7,9] As always, caution patients about driving or drinking alcohol.

ROCHE®

nights of sleep...

DALMANE®

flurazepam HCl/Roche ⓒ

sleep that satisfies

Please see following page for references and summary of product information

References: **1.** Kales J, *et al: Clin Pharmacol Ther 12*:691-697, Jul-Aug 1971. **2.** Kales A, *et al: Clin Pharmacol Ther 18*:356-363, Sep 1975. **3.** Kales A, *et al: Clin Pharmacol Ther 19*:576-583, May 1976. **4.** Kales A, *et al: Clin Pharmacol Ther 32*:781-788, Dec 1982. **5.** Frost JD Jr, DeLucchi MR: *J Am Geriatr Soc 27*:541-546, Dec 1979. **6.** Dement WC, *et al: Behav Med*, pp. 25-31, Oct 1978. **7.** Kales A, Kales JD: *J Clin Psychopharmacol 3*:140-150, Apr 1983. **8.** Tennant FS, *et al:* Symposium on the Treatment of Sleep Disorders, Teleconference, Oct 16, 1984. **9.** Greenblatt DJ, Allen MD, Shader RI: *Clin Pharmacol Ther 21*:355-361, Mar 1977.

See following page.

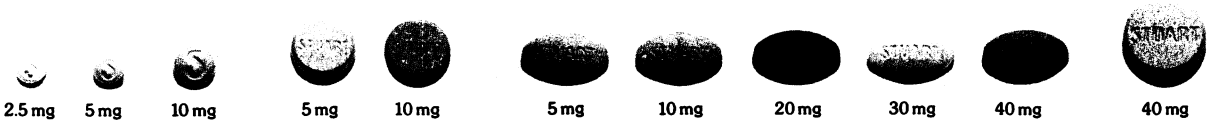
Angina comes in many forms...

So does

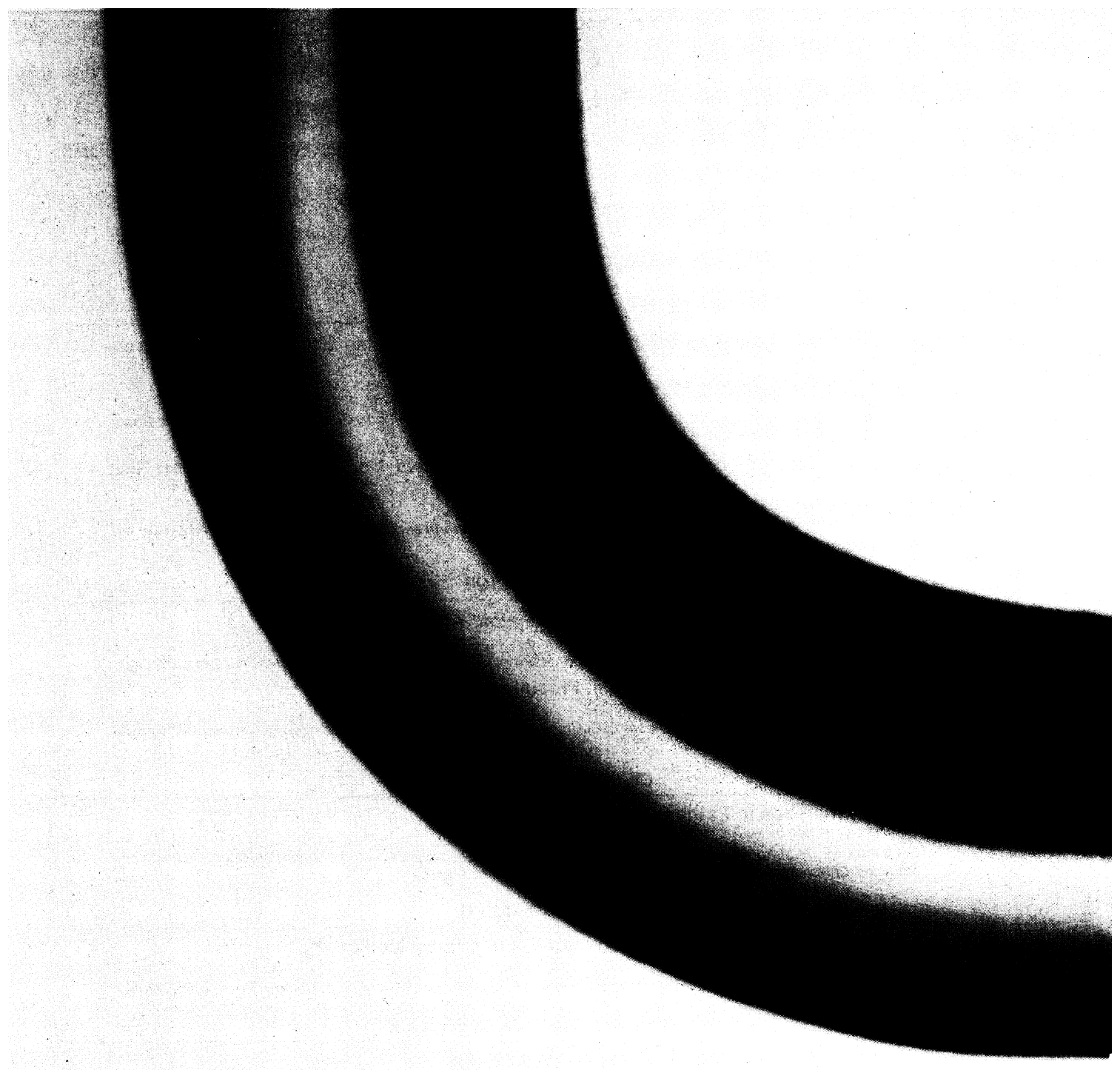
SORBITRATE®

(ISOSORBIDE DINITRATE)

Unsurpassed flexibility in nitrate therapy.



See previous page for brief summary of prescribing information.



"With [CAPOTEN® (captopril tablets)] it appears that for the first time ever a patient can feel as well on treatment for high blood pressure as he does off it."[1]

*Angiotensin Converting Enzyme

†CAPOTEN may be used as initial therapy only for patients with normal renal function in whom the risk of neutropenia/agranulocytosis is relatively low (1 out of over 8,600 in clinical trials). Use special precautions in patients with impaired renal function, collagen vascular disorders, or those exposed to other drugs known to affect the white cells or immune response. Evaluation of hypertensives should always include assessment of renal function. See INDICATIONS, WARNINGS, and ADVERSE REACTIONS in the brief summary on the adjacent page.

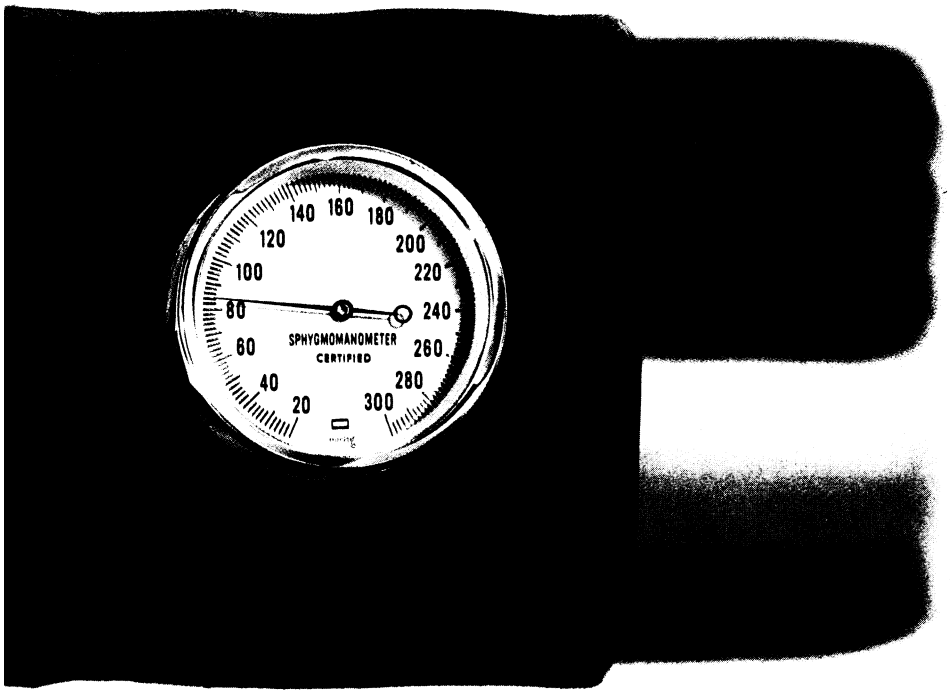
‡The most frequently occurring adverse reactions are skin rash and taste alteration; both effects are generally mild, reversible, or self-limited.

Reference:

1. Stumpe KO, Overlack A, Kolloch R, et al: Long-term efficacy of angiotensin-converting-enzyme inhibition with captopril in mild-to-moderate essential hypertension. Br J Clin Pharmacol 14(suppl 2):121S-126S, 1982.

New Prescribing Freedom–
Mild-to-Moderate Hypertension

Capoten Now for All Degrees of Hypertension



- ☐ Now for <u>initial</u> therapy of hypertension†
- ☐ Effective <u>alone</u> or in combination with diuretics
- ☐ Fatigue, loss of libido, impotence, and mental impairment <u>almost never</u> occur‡
- ☐ <u>Convenient</u> bid dosage

*ACE*INHIBITOR*

CAPOTEN®

captopril tablets

HELP PUT QUALITY BACK INTO LIVING

SQUIBB®

CAPOTEN® TABLETS
Captopril Tablets

INDICATIONS: Hypertension – CAPOTEN (captopril) is indicated for the treatment of hypertension. Consideration should be given to the risk of neutropenia/agranulocytosis (see WARNINGS). CAPOTEN may be used as initial therapy for patients with normal renal function, in whom the risk is relatively low. In patients with impaired renal function, particularly those with collagen vascular disease, captopril should be reserved for those who have either developed unacceptable side effects on other drugs, or have failed to respond satisfactorily to drug combinations. CAPOTEN is effective alone and in combination with other antihypertensive agents, especially thiazide-type diuretics.

Heart Failure: CAPOTEN (captopril) is indicated in patients with heart failure who have not responded adequately to or cannot be controlled by conventional diuretic and digitalis therapy. CAPOTEN is to be used with diuretics and digitalis.

WARNINGS: Neutropenia/Agranulocytosis – Neutropenia ($< 1000/mm^3$) with myeloid hypoplasia has resulted from use of captopril. About half of the neutropenic patients developed systemic or oral cavity infections or other features of the syndrome of agranulocytosis. The risk of neutropenia is dependent on the clinical status of the patient:

In clinical trials in patients with hypertension who have normal renal function (serum creatinine < 1.6 mg/dL and no collagen disease), neutropenia has been seen in one patient out of over 8,600 exposed. In patients with some degree of renal failure (serum creatinine at least 1.6 mg/dL) but no collagen vascular disease, the risk in clinical trials was about 1 per 500. Doses were relatively high in these patients, particularly in view of their diminished renal function. In patients with collagen vascular diseases (e.g., systemic lupus erythematosus, scleroderma) and impaired renal function, neutropenia occurred in 3.7% of patients in clinical trials. While none of the over 750 patients in formal clinical trials of heart failure developed neutropenia, it has occurred during subsequent clinical experience. Of reported cases, about half had serum creatinine ≥ 1.6 mg/dL and more than 75% received procainamide. In heart failure, it appears that the same risk factors for neutropenia are present.

Neutropenia has appeared within 3 months after starting therapy, associated with myeloid hypoplasia and frequently accompanied by erythroid hypoplasia and decreased numbers of megakaryocytes (e.g., hypoplastic bone marrow and pancytopenia); anemia and thrombocytopenia were sometimes seen. Neutrophils generally returned to normal in about 2 weeks after captopril was discontinued, and serious infections were limited to clinically complex patients. About 13% of the cases of neutropenia have ended fatally, but almost all fatalities were in patients with serious illness, having collagen vascular disease, renal failure, heart failure or immunosuppressant therapy, or a combination of these complicating factors.

Evaluation of the hypertensive or heart failure patient should always include assessment of renal function. If captopril is used in patients with impaired renal function, white blood cell and differential counts should be evaluated prior to starting treatment and at approximately 2-week intervals for about 3 months, then periodically. In patients with collagen vascular disease or who are exposed to other drugs known to affect the white cells or immune response, particularly when there is impaired renal function, captopril should be used only after an assessment of benefit and risk, and then with caution. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat, fever); if infection is suspected, perform counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count $< 1000/mm^3$) withdraw captopril and closely follow the patient's course.

Proteinuria – Total urinary proteins >1 g/day were seen in about 0.7% of patients on captopril. About 90% of affected patients had evidence of prior renal disease or received high doses (>150 mg/day), or both. The nephrotic syndrome occurred in about one-fifth of proteinuric patients. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatinine were seldom altered in proteinuric patients. Since most cases of proteinuria occurred by the 8th month of therapy, patients with prior renal disease or those receiving captopril at doses >150 mg/day should have urinary protein estimates (dip-stick on 1st morning urine) before therapy, and periodically thereafter.

Hypotension – Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salt/volume-depleted persons such as those treated vigorously with diuretics (see PRECAUTIONS [Drug Interactions]).

In heart failure, where blood pressure was either normal or low, transient decreases in mean blood pressure >20% were recorded in about half of the patients. This transient hypotension may occur after any of the first several doses and is usually well tolerated, although rarely it has been associated with arrhythmia or conduction defects. A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first 2 weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.

PRECAUTIONS: General: *Impaired Renal Function,* Hypertension – Some hypertensive patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible. Heart Failure – About 20% of patients develop stable elevations of BUN and serum creatinine >20% above normal or baseline upon long-term treatment. Less than 5% of patients, generally with severe preexisting renal disease, required discontinuation due to progressively increasing creatinine. See DOSAGE AND ADMINISTRATION, ADVERSE REACTIONS [Altered Laboratory Findings]. *Valvular Stenosis* – A theoretical concern, for risk of decreased coronary perfusion, has been noted regarding vasodilator treatment in patients with aortic stenosis due to decreased afterload reduction.

Surgery/Anesthesia – If hypotension occurs during major surgery or anesthesia, and is considered due to the effects of captopril, it is correctable by volume expansion.

Drug Interactions: *Hypotension: Patients on Diuretic Therapy* – Precipitous reduction of blood pressure may occasionally occur within the 1st hour after administration of the initial captopril dose in patients on diuretics, especially those recently placed on diuretics, and those on severe dietary salt restriction or dialysis. This possibility can be minimized by either discontinuing the diuretic or increasing the salt intake about 1 week prior to initiation of captopril therapy or by initiating therapy with small doses (6.25 or 12.5 mg). Alternatively, provide medical supervision for at least 1 hour after the initial dose.

Agents Having Vasodilator Activity – In heart failure patients, vasodilators should be administered with caution.

Agents Causing Renin Release – Captopril's effect will be augmented by antihypertensive agents that cause renin release.

Agents Affecting Sympathetic Activity – The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril alone or with diuretics. Beta-adrenergic blocking drugs add some further antihypertensive effect to captopril, but the overall response is less than additive. Therefore, use agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) with caution.

Agents Increasing Serum Potassium – Give potassium-sparing diuretics or potassium supplements only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium. Use potassium-containing salt substitutes with caution.

Inhibitors of Endogenous Prostaglandin Synthesis – Indomethacin and other nonsteroidal anti-inflammatory agents may reduce the antihypertensive effect of captopril, especially in low renin hypertension.

Drug/Laboratory Test Interaction: Captopril may cause a false-positive urine test for acetone.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Two-year studies with doses of 50 to 1350 mg/kg/day in mice and rats failed to show any evidence of carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Pregnancy: Category C – There are no adequate and well-controlled studies in pregnant women. Embryocidal effects were observed in rabbits. Therefore, captopril should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus. Captopril crosses the human placenta.

Nursing Mothers: Captopril is secreted in human milk. Exercise caution when administering captopril to a nursing woman, and, in general, nursing should be interrupted.

Pediatric Use: Safety and effectiveness in children have not been established although there is limited experience with use of captopril in children from 2 months to 15 years of age. Dosage, on a weight basis, was comparable to that used in adults. Captopril should be used in children only if other measures for controlling blood pressure have not been effective.

ADVERSE REACTIONS: Reported incidences are based on clinical trials involving approximately 7000 patients.

Renal – About 1 of 100 patients developed proteinuria (see WARNINGS). Renal insufficiency, renal failure, polyuria, oliguria, and urinary frequency in 1 to 2 of 1000 patients.

Hematologic – Neutropenia/agranulocytosis have occurred (see WARNINGS). Anemia, thrombocytopenia, and pancytopenia have been reported.

Dermatologic – Rash (usually maculopapular, rarely urticarial), often with pruritus and sometimes with fever and eosinophilia, in about 4 to 7 of 100 patients (depending on renal status and dose), usually during the 1st 4 weeks of therapy. Pruritus, without rash, in about 2 of 100 patients. A reversible associated pemphigoid-like lesion, and photosensitivity have also been reported. Angioedema of the face, mucous membranes of the mouth, or of the extremities in about 1 of 1000 patients – reversible on discontinuance of captopril therapy. One case of laryngeal edema reported. Flushing or pallor in 2 to 5 of 1000 patients.

Cardiovascular – Hypotension may occur, see WARNINGS and PRECAUTIONS (Drug Interactions) for discussion of hypotension on initiation of captopril therapy. Tachycardia, chest pain, and palpitations each in about 1 of 100 patients. Angina pectoris, myocardial infarction, Raynaud's syndrome, and congestive heart failure each in 2 to 3 of 1000 patients.

Dysgeusia – About 2 to 4 (depending on renal status and dose) of 100 patients developed a diminution or loss of taste perception; taste impairment is reversible and usually self-limited even with continued drug use (2 to 3 months). Gastric irritation, abdominal pain, nausea, vomiting, diarrhea, anorexia, constipation, aphthous ulcers, peptic ulcer, dizziness, headache, malaise, fatigue, insomnia, dry mouth, dyspnea, cough, alopecia, and paresthesias reported in about 0.5 to 2% of patients but did not appear at increased frequency compared to placebo or other treatments used in controlled trials.

Altered Laboratory Findings: Elevations of liver enzymes in a few patients although no causal relationship has been established. Rarely cholestatic jaundice and hepatocellular injury with or without secondary cholestasis, have been reported. A transient elevation of BUN and serum creatinine may occur, especially in volume-depleted or renovascular hypertensive patients. In instances of rapid reduction of longstanding or severely elevated blood pressure, the glomerular filtration rate may decrease transiently, also resulting in transient rises in serum creatinine and BUN. Small increases in serum potassium concentration frequently occur, especially in patients with renal impairment (see PRECAUTIONS).

OVERDOSAGE: Primary concern is correction of hypotension. Volume expansion with an I.V. infusion of normal saline is the treatment of choice for restoration of blood pressure. Captopril may be removed from the general circulation by hemodialysis.

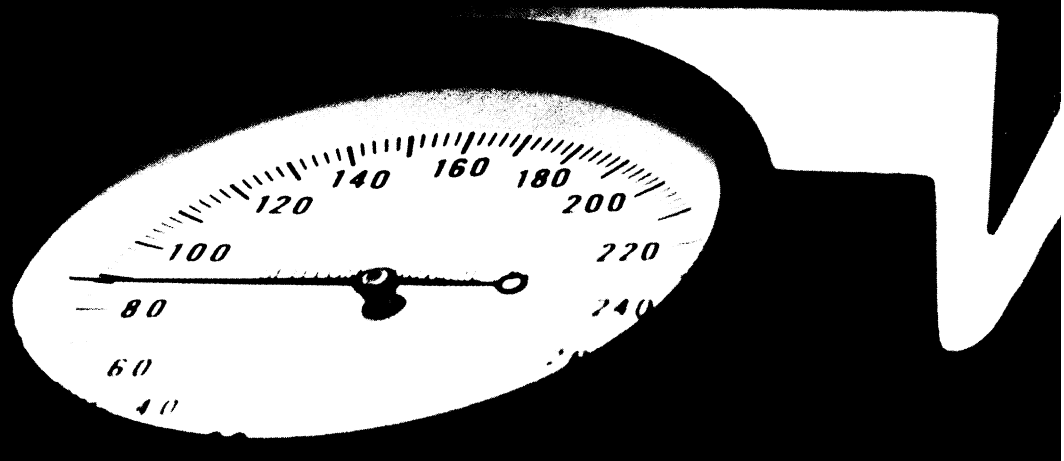
DOSAGE AND ADMINISTRATION: CAPOTEN (captopril) should be taken one hour before meals. In hypertension, CAPOTEN may be dosed bid or tid. Dosage must be individualized; see DOSAGE AND ADMINISTRATION section of package insert for detailed information regarding dosage in hypertension and in heart failure. Because CAPOTEN (captopril) is excreted primarily by the kidneys, dosage adjustments are recommended for patients with impaired renal function.

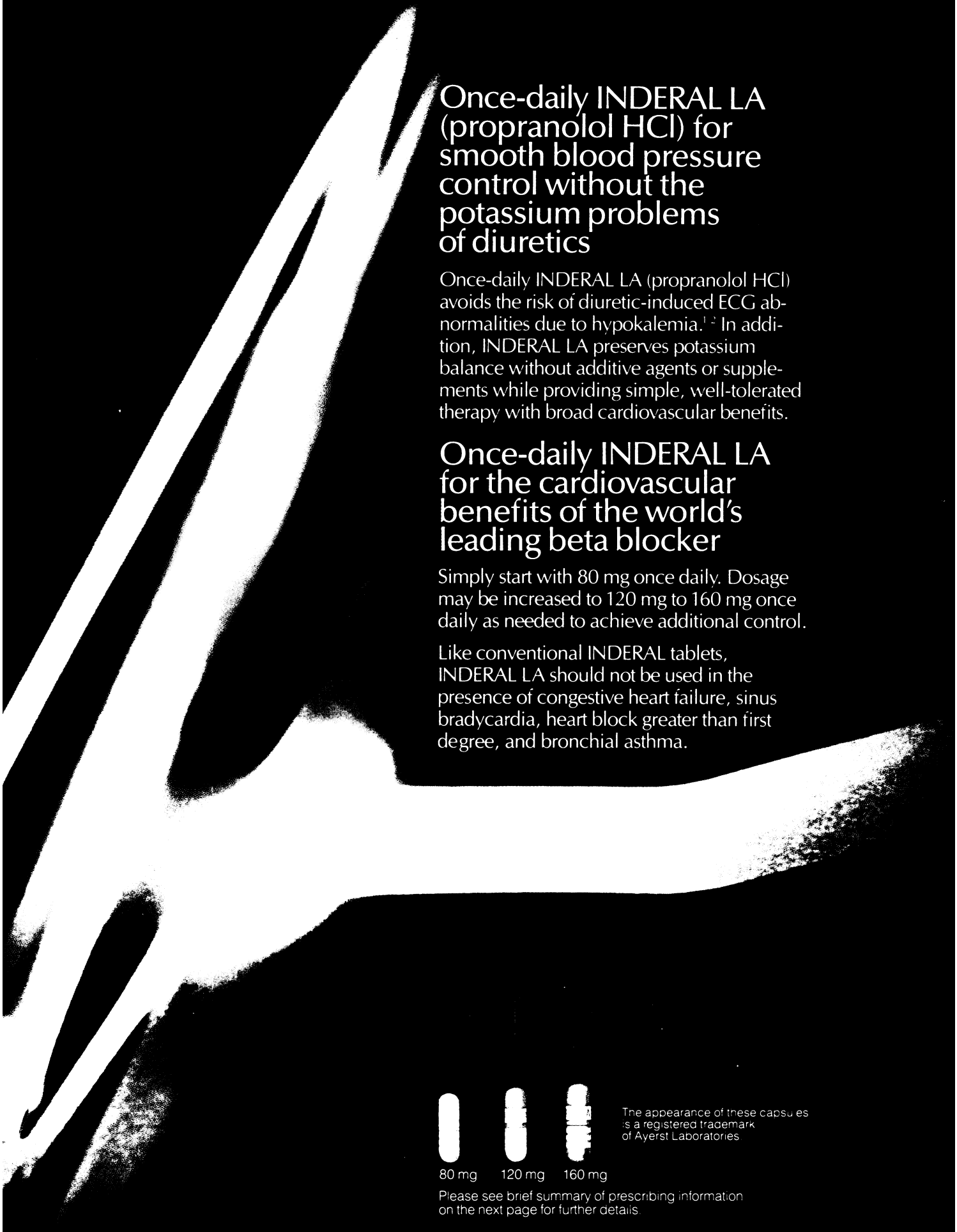
Consult package insert before prescribing CAPOTEN (captopril).

HOW SUPPLIED: Available in tablets of 12.5, 25, 50, and 100 mg in bottles of 100 (25 mg also available in bottles of 1000), and in UNIMATIC® single dose packs of 100 tablets.
(J3-658C)

 525-566 Issued: August 1985

Right from the start in hypertension...





Once-daily INDERAL LA (propranolol HCl) for smooth blood pressure control without the potassium problems of diuretics

Once-daily INDERAL LA (propranolol HCl) avoids the risk of diuretic-induced ECG abnormalities due to hypokalemia.[1,2] In addition, INDERAL LA preserves potassium balance without additive agents or supplements while providing simple, well-tolerated therapy with broad cardiovascular benefits.

Once-daily INDERAL LA for the cardiovascular benefits of the world's leading beta blocker

Simply start with 80 mg once daily. Dosage may be increased to 120 mg to 160 mg once daily as needed to achieve additional control.

Like conventional INDERAL tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, heart block greater than first degree, and bronchial asthma.

80 mg 120 mg 160 mg

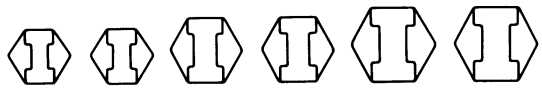
The appearance of these capsules is a registered trademark of Ayerst Laboratories

Please see brief summary of prescribing information on the next page for further details.

"When it comes to cardiovascular medicine, I like to know exactly what my patients are swallowing."

INDERAL® Tablets

BRAND OF PROPRANOLOL HCl



10 mg 20 mg 40 mg 60 mg 80 mg 90 mg*

BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)

INDERAL® (propranolol hydrochloride) Tablets

CONTRAINDICATIONS

INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS

CARDIAC FAILURE: Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)—PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY: The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL, like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA: Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS: Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS

General: Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL (propranolol hydrochloride) may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

Clinical Laboratory Tests: Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS: Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy: Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular: bradycardia; congestive heart failure; intensification of AV block; hypotension; paresthesia of hands; thrombocytopenic purpura; arterial insufficiency, usually of the Raynaud type.

Central Nervous System: Lightheadedness; mental depression manifested by insomnia, lassitude, weakness, fatigue; reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal: nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic: pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory: bronchospasm.

Hematologic: agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

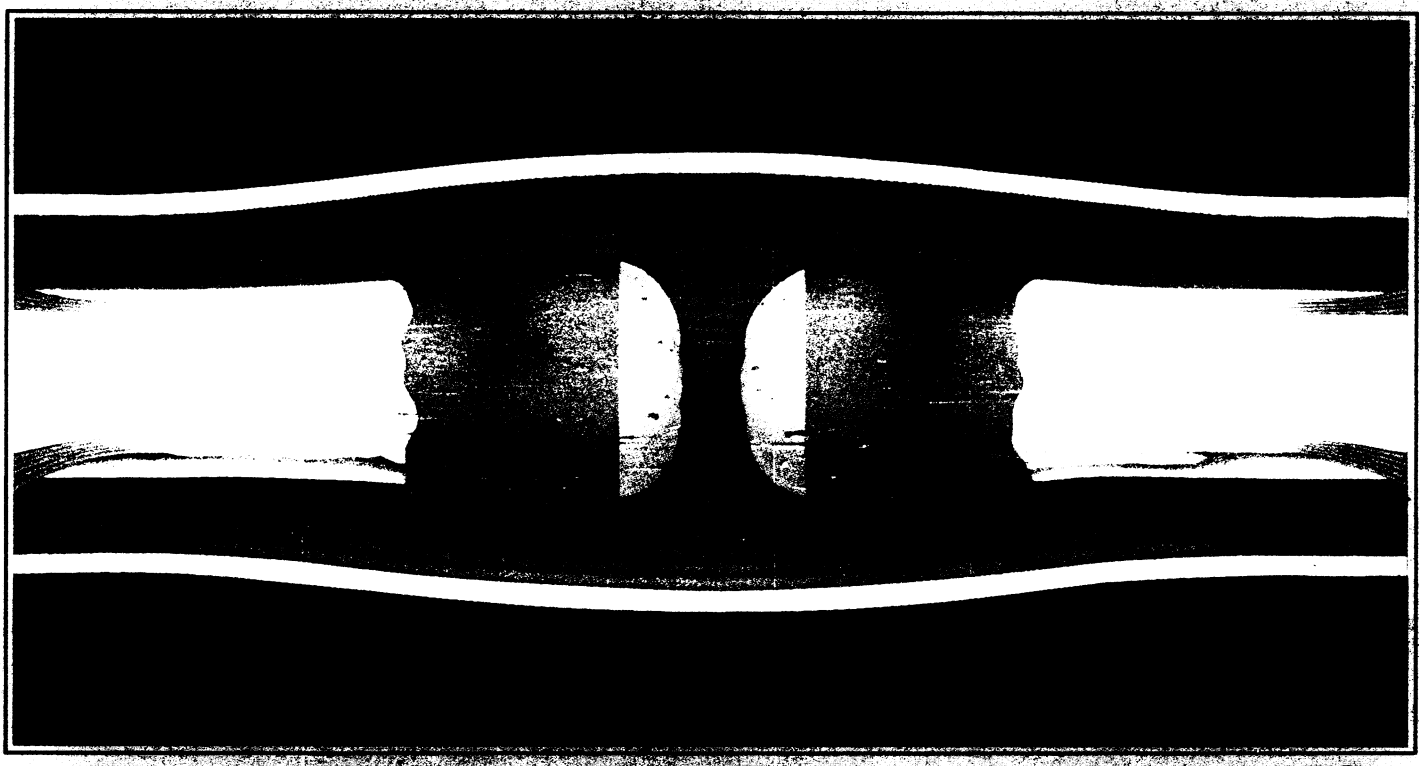
Auto-Immune: In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous: alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

*The appearance of INDERAL tablets is a registered trademark of Ayerst Laboratories.

9429/185

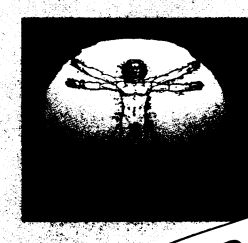
Ayerst® AYERST LABORATORIES
New York, N.Y. 10017



When the pain and inflammation of arthritis flare up...

- FELDENE is an excellent choice for osteoarthritis and rheumatoid arthritis. Beginning with the first dose, FELDENE provides effective and long-lasting relief of arthritis pain and stiffness.[1]
- Convenient once-daily dosage provides round-the-clock relief of symptoms[2]—encouraging compliance and enhancing productivity at home and on the job.[3]

Feldene®
(PIROXICAM) 20 mg capsules



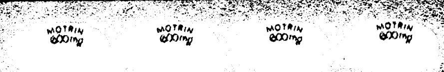
Please see a brief summary of FELDENE (piroxicam) prescribing information on the following page.

NOW ON **Medi-Cal**

Feldene®

(PIROXICAM) 20 mg capsules

Prescribe one 20mg capsule daily for convenience and compliance



Source: PDR, [illegible] Manufacturers' Prescribing Information.

Indicates maximum dosage for osteoarthritis and rheumatoid arthritis for the [illegible]

Brief Summary

FELDENE® (piroxicam) Capsules

CONTRAINDICATIONS: FELDENE (piroxicam) should not be used in patients who have previously [illegible] hypersensitivity to it, or in individuals with [illegible] polyps and angioedema [illegible]

WARNINGS: [illegible] and, in some instances, fatal—have been reported with [illegible] FELDENE. If FELDENE must be given to patients with a history of upper gastrointestinal tract disease, the patient should be under close supervision (see ADVERSE REACTIONS).

PRECAUTIONS: As with other anti-inflammatory agents, long-term administration to animals results in renal papillary necrosis and related pathology in [illegible]

Acute renal failure and hyperkalemia as well as [illegible] have been reported with FELDENE. In addition to [illegible] papillary necrosis and the nephrotic syndrome have been reported with FELDENE.

Although other nonsteroidal [illegible] aspirin does, all drugs [illegible] to some degree.

Because of reports of adverse eye findings with nonsteroidal anti-inflammatory agents, it is recommended that patients who develop visual complaints during treatment with FELDENE have ophthalmic evaluation.

As with other nonsteroidal anti-inflammatory [illegible] in up to 15% of patients. [illegible] reaction while on therapy [illegible]

Severe hepatic reactions, [illegible] have been reported with FELDENE. Although such reactions are rare, if [illegible] consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), FELDENE should be discontinued. (See also ADVERSE REACTIONS.)

Although at the recommended dose of 20 mg/day of FELDENE increased fecal blood loss due to gastrointestinal irritation did not occur, in about 4% of the patients treated with FELDENE alone or concomitantly with aspirin, reductions in hemoglobin and hematocrit values were observed.

Peripheral edema has been observed in [illegible] 2% of the patients treated with FELDENE. Therefore, FELDENE should be used with caution in [illegible] heart failure, hypertension or other conditions predisposing to fluid retention.

A combination of dermatological [illegible] symptoms suggestive of serum sickness have occasionally occurred in conjunction with [illegible] FELDENE. These include arthralgias, pruritus, fever, fatigue, and rash including [illegible]

DRUG INTERACTIONS: Interactions with [illegible] anticoagulants have been reported with FELDENE since marketing. Therefore, physicians should closely monitor patients for a change in dosage requirements when administering FELDENE to patients on [illegible]

Plasma levels of piroxicam are depressed to approximately 80% of their normal values when FELDENE is administered in conjunction with aspirin (3900 mg/day), but concomitant administration of antacids has no effect on piroxicam plasma levels.

Nonsteroidal anti-inflammatory agents, including FELDENE, have been reported to increase steady state plasma lithium levels. It is recommended that plasma lithium levels be monitored when initiating, adjusting and discontinuing FELDENE.

Carcinogenesis, [illegible] and chronic toxicity studies have been carried out in rats, [illegible]

The pathology most often seen was that characteristically associated with the animal toxicology of anti-inflammatory agents: renal papillary [illegible] lesions.

In classical studies in [illegible] did not show any teratogenic potential.

Reproductive studies [illegible] in animals.

[illegible] piroxicam [illegible] rition in animals. [illegible] in pregnant animals in the last trimester of pregnancy compared to non-pregnant [illegible] trimesters of pregnancy.

FELDENE is not recommended for use in nursing mothers or in pregnant women because of the animal findings and since safety for such use has not been established in humans.

Use in Children: Dosage recommendations and indications for use in children have not been established.

ADVERSE REACTIONS: Gastrointestinal [illegible] the most prominent side effects, occurring in approximately 20% of the patients, which in most [illegible] interfere with the course of therapy. Of the patients experiencing gastrointestinal side effects, approximately 5% discontinued therapy with an overall incidence of peptic ulceration of about 1%.

Adverse reactions are listed below by body system for all patients in clinical trials with FELDENE at doses of 20 mg/day.

Incidence Greater Than 1%: The following adverse reactions occurred more frequently than 1 in 100.

Gastrointestinal: stomatitis, anorexia, epigastric distress,* nausea,* constipation, abdominal discomfort, [illegible]

[illegible]

References: 1 Siegmeth W: Serum concentrations of piroxicam in relation to its clinical effect in patients with [illegible] polyarthritis. *Wien Med Wochenschr* (special [illegible]) [illegible] 1980. 2. [illegible] piroxicam in the treatment of rheumatoid arthritis. [illegible] 72:18-22, February 1982. 3. [illegible] Quality of life as a measure of therapeutic response. [illegible] (special suppl):37-43, 1984.

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The Scientific Program at the 1986 Canada West Medical Congress has been approved for 26 hours study credit by the College of Family Physicians of Canada and, through a reciprocal agreement, by the American Academy of Family Physicians. Application has been made to the American Medical Association.

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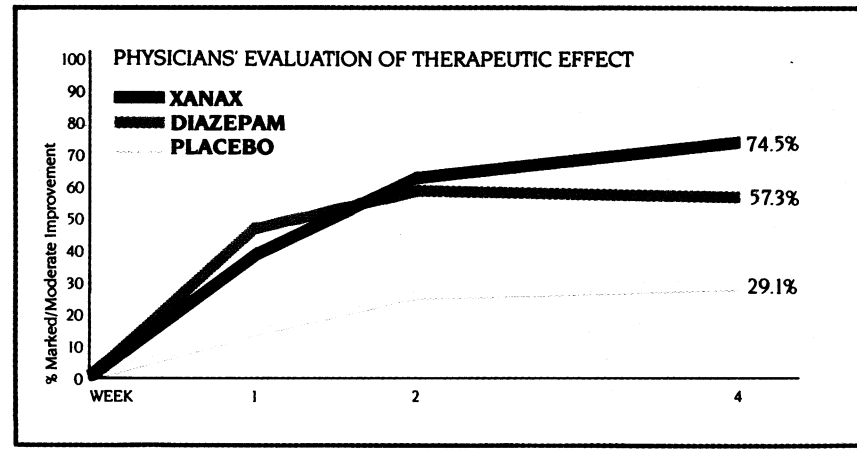
FOR CLINICAL ANXIETY

EFFICACY EQUAL TO DIAZEPAM WITH LESS DROWSINESS

In double-blind, placebo-controlled clinical trials in 976 patients with moderate to severe clinical anxiety, therapy with XANAX was compared to diazepam.*

Patients treated with XANAX *had a significantly lower incidence of drowsiness when compared directly to diazepam* therapy in *a 976-patient*, placebo-controlled, multicenter study.*

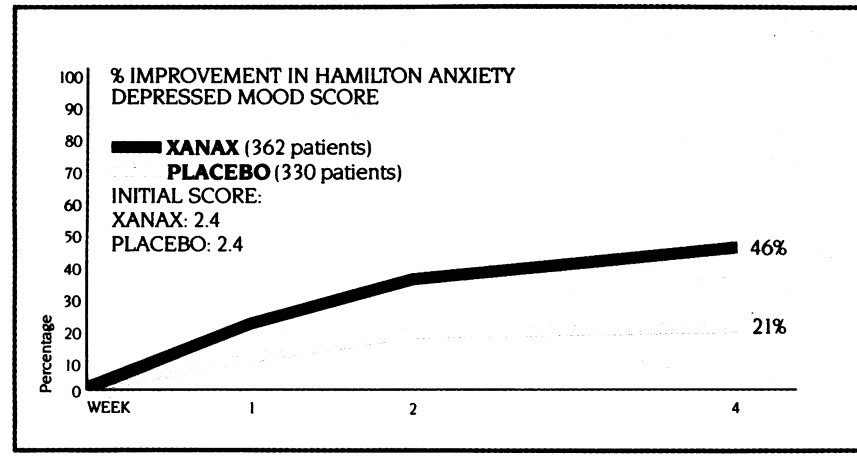


AND CLINICAL ANXIETY WITH DEPRESSIVE SYMPTOMS

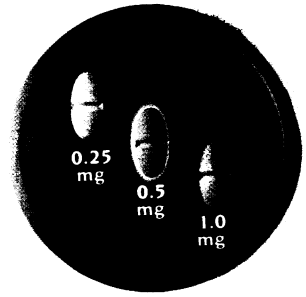
EFFECTIVE IN CLINICAL ANXIETY WITH DEPRESSIVE SYMPTOMS

Patients with clinical anxiety may complain of having feelings of depression, such as sadness, blueness, or loneliness.

Depressed mood is one of 14 items on the Hamilton Anxiety Rating Scale. Special analysis of 692 anxious patients with a significant depressed mood item score showed that treatment with XANAX was significantly better than placebo in decreasing depressed mood score.



SIMPLE DOSAGE: XANAX 0.25–0.5 mg T.I.D.



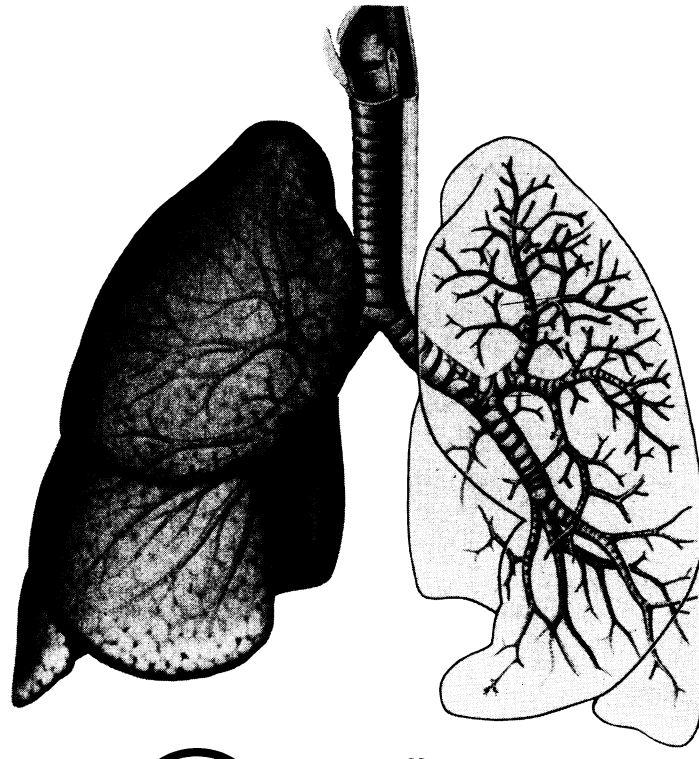
The usual starting dose of XANAX is 0.25 to 0.5 mg, three times daily.

Please see next page for brief summary of prescribing information.

Xanax® 0.5 mg Tablets

alprazolam Ⓒ

Consider the causative organisms...



Ceclor®
cefaclor
250-mg Pulvules® t.i.d.

offers effectiveness against the major causes of bacterial bronchitis

H. influenzae*, *H. influenzae*, *S. pneumoniae*, *S. pyogenes
(ampicillin-susceptible) (ampicillin-resistant)

Brief Summary. Consult the package literature for prescribing information.

Indications and Usage: Ceclor* (cefaclor, Lilly) is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

Lower respiratory infections, including pneumonia caused by *Streptococcus pneumoniae (Diplococcus pneumoniae), Haemophilus influenzae,* and *S. pyogenes* (group A beta-hemolytic streptococci)

Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to Ceclor.

Contraindication: Ceclor is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

Warnings: IN PENICILLIN-SENSITIVE PATIENTS, CEPHALOSPORIN ANTIBIOTICS SHOULD BE ADMINISTERED CAUTIOUSLY. THERE IS CLINICAL AND LABORATORY EVIDENCE OF PARTIAL CROSS-ALLERGENICITY OF THE PENICILLINS AND THE CEPHALOSPORINS, AND THERE ARE INSTANCES IN WHICH PATIENTS HAVE HAD REACTIONS, INCLUDING ANAPHYLAXIS, TO BOTH DRUG CLASSES.

Antibiotics, including Ceclor, should be administered cautiously to any patient who has demonstrated some form of allergy, particularly to drugs.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics (including macrolides, semisynthetic penicillins, and cephalosporins); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening.

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.

Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, management should include sigmoidoscopy, appropriate bacteriologic studies, and fluid, electrolyte, and protein supplementation. When the colitis does not improve after the drug has been discontinued, or when it is severe, oral vancomycin is the drug of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile.* Other causes of colitis should be ruled out.

Precautions: *General Precautions* — If an allergic reaction to Ceclor* (cefaclor, Lilly) occurs, the drug should be discontinued, and, if necessary, the patient should be treated with appropriate agents, e.g., pressor amines, antihistamines, or corticosteroids.

Prolonged use of Ceclor may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

Ceclor should be administered with caution in the presence of markedly impaired renal function. Under such conditions, careful clinical observation and laboratory studies should be made because safe dosage may be lower than that usually recommended.

As a result of administration of Ceclor, a false-positive reaction for glucose in the urine may occur. This has been observed with Benedict's and Fehling's solutions and also with Clinitest® tablets but not with Tes-Tape® (Glucose Enzymatic Test Strip, USP, Lilly).

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Usage in Pregnancy — Pregnancy Category B — Reproduction studies have been performed in mice and rats at doses up to 12 times the human dose and in ferrets given three times the maximum human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Ceclor® (cefaclor, Lilly). There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers — Small amounts of Ceclor have been detected in mother's milk following administration of single 500-mg doses. Average levels were 0.18, 0.20, 0.21, and 0.16 mcg/ml at two, three, four, and five hours respectively. Trace amounts were detected at one hour. The effect on nursing infants is not known. Caution should be exercised when Ceclor is administered to a nursing woman.

Usage in Children — Safety and effectiveness of this product for use in infants less than one month of age have not been established.

Adverse Reactions: Adverse effects considered related to therapy with Ceclor are uncommon and are listed below:

Gastrointestinal symptoms occur in about 2.5 percent of patients and include diarrhea (1 in 70).

Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

Hypersensitivity reactions have been reported in about 1.5 percent of patients and include morbiliform eruptions (1 in 100). Pruritus, urticaria, and positive Coombs' tests each occur in less than 1 in 200 patients. Cases of serum-sickness-like reactions (erythema multiforme or the above skin manifestations accompanied by arthritis/arthralgia and, frequently, fever) have been reported. These reactions are apparently due to hypersensitivity and have usually occurred during or following a second course of therapy with Ceclor. Such reactions have been reported more frequently in children than in adults. Signs and symptoms usually occur a few days after initiation of therapy and subside within a few days after cessation of therapy. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.

Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.

Other effects considered related to therapy included eosinophilia (1 in 50 patients) and genital pruritus or vaginitis (less than 1 in 100 patients).

Causal Relationship Uncertain — Transitory abnormalities in clinical laboratory test results have been reported. Although they were of uncertain etiology, they are listed below to serve as alerting information for the physician.

Hepatic — Slight elevations in SGOT, SGPT, or alkaline phosphatase values (1 in 40).

Hematopoietic — Transient fluctuations in leukocyte count, predominantly lymphocytosis occurring in infants and young children (1 in 40).

Renal — Slight elevations in BUN or serum creatinine (less than 1 in 500) or abnormal urinalysis (less than 1 in 200).

[061782R]

Note: Ceclor® (cefaclor, Lilly) is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

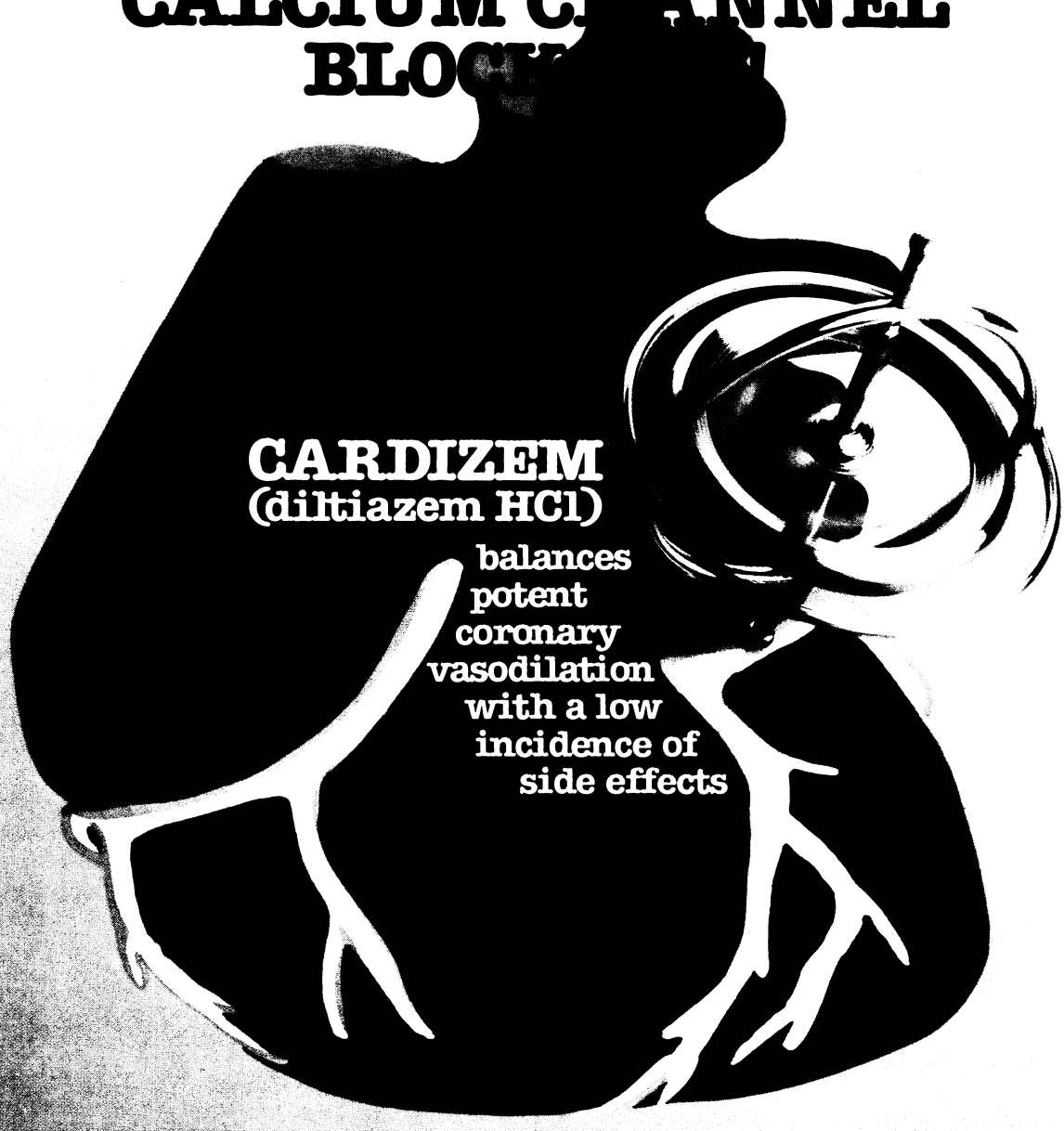
Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285.

Eli Lilly Industries, Inc.
Carolina, Puerto Rico 00630

400441

BALANCED CALCIUM CHANNEL BLOCKER



CARDIZEM
(diltiazem HCl)

balances potent coronary vasodilation with a low incidence of side effects

Low incidence of side effects
CARDIZEM® (diltiazem HCl) produces an incidence of adverse reactions not greater than that reported with placebo therapy, thus contributing to the patient's sense of well-being.

[illegible] indicated for the treatment of angina pectoris due to coronary artery spasm and in the management of chronic stable angina (effort-associated angina) in patients who cannot [illegible] and/or nitrates or who remain [illegible] doses of these agents.

[illegible] Safety and efficacy [illegible] for the treatment of stable angina [illegible] Am J Cardiol

[illegible] the treatment of exercise-[illegible] effects on treadmill [illegible]

Reduces angina attack frequency*
42% to 46% decrease reported in multicenter study.[1]

Increases exercise tolerance*
In Bruce exercise test,[2] control patients averaged 8.0 minutes to onset of pain; Cardizem patients averaged 9.8 minutes ($P<.005$).

CARDIZEM®
(diltiazem HCl)

THE BALANCED CALCIUM CHANNEL BLOCKER

Please see full prescribing information on following page.

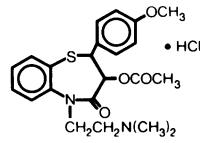
2/84

PROFESSIONAL USE INFORMATION

cardizem®
(diltiazem HCl)
30 mg and 60 mg tablets

DESCRIPTION

CARDIZEM® (diltiazem hydrochloride) is a calcium ion influx inhibitor (slow channel blocker or calcium antagonist). Chemically, diltiazem hydrochloride is 1,5-Benzothiazepin-4(5H)one,3-(acetyloxy) -5-[2-(dimethylamino)ethyl]-2,3-dihydro-2-(4-methoxyphenyl)-, monohydrochloride,(+) -cis-. The chemical structure is:



Diltiazem hydrochloride is a white to off-white crystalline powder with a bitter taste. It is soluble in water, methanol, and chloroform. It has a molecular weight of 450.98. Each tablet of CARDIZEM contains either 30 mg or 60 mg diltiazem hydrochloride for oral administration.

CLINICAL PHARMACOLOGY

The therapeutic benefits achieved with CARDIZEM are believed to be related to its ability to inhibit the influx of calcium ions during membrane depolarization of cardiac and vascular smooth muscle.

Mechanisms of Action. Although precise mechanisms of its antianginal actions are still being delineated, CARDIZEM is believed to act in the following ways:

1. Angina Due to Coronary Artery Spasm: CARDIZEM has been shown to be a potent dilator of coronary arteries both epicardial and subendocardial. Spontaneous and ergonovine-induced coronary artery spasm are inhibited by CARDIZEM.
2. Exertional Angina: CARDIZEM has been shown to produce increases in exercise tolerance, probably due to its ability to reduce myocardial oxygen demand. This is accomplished via reductions in heart rate and systemic blood pressure at submaximal and maximal exercise work loads.

In animal models, diltiazem interferes with the slow inward (depolarizing) current in excitable tissue. It causes excitation-contraction uncoupling in various myocardial tissues without changes in the configuration of the action potential. Diltiazem produces relaxation of coronary vascular smooth muscle and dilation of both large and small coronary arteries at drug levels which cause little or no negative inotropic effect. The resultant increases in coronary blood flow (epicardial and subendocardial) occur in ischemic and nonischemic models and are accompanied by dose-dependent decreases in systemic blood pressure and decreases in peripheral resistance.

Hemodynamic and Electrophysiologic Effects. Like other calcium antagonists, diltiazem decreases sinoatrial and atrioventricular conduction in isolated tissues and has a negative inotropic effect in isolated preparations. In the intact animal, prolongation of the AH interval can be seen at higher doses.

In man, diltiazem prevents spontaneous and ergonovine-provoked coronary artery spasm. It causes a decrease in peripheral vascular resistance and a modest fall in blood pressure and, in exercise tolerance studies in patients with ischemic heart disease, reduces the heart rate-blood pressure product for any given work load. Studies to date, primarily in patients with good ventricular function, have not revealed evidence of a negative inotropic effect; cardiac output, ejection fraction, and left ventricular end diastolic pressure have not been affected. There are as yet few data on the interaction of diltiazem and beta-blockers. Resting heart rate is usually unchanged or slightly reduced by diltiazem.

Intravenous diltiazem in doses of 20 mg prolongs AH conduction time and AV node functional and effective refractory periods approximately 20%. In a study involving single oral doses of 300 mg of CARDIZEM in six normal volunteers, the average maximum PR prolongation was 14% with no instances of greater than first-degree AV block. Diltiazem-associated prolongation of the AH interval is not more pronounced in patients with first-degree heart block. In patients with sick sinus syndrome, diltiazem significantly prolongs sinus cycle length (up to 50% in some cases).

Chronic oral administration of CARDIZEM in doses of up to 240 mg/day has resulted in small increases in PR interval, but has not usually produced abnormal prolongation. There were, however, three instances of second-degree AV block and one instance of third-degree AV block in a group of 959 chronically treated patients.

Pharmacokinetics and Metabolism. Diltiazem is absorbed from the tablet formulation to about 80% of a reference capsule and is subject to an extensive first-pass effect, giving an absolute bioavailability (compared to intravenous dosing) of about 40%. CARDIZEM undergoes extensive hepatic metabolism in which 2% to 4% of the unchanged drug appears in the urine. In vitro binding studies show CARDIZEM is 70% to 80% bound to plasma proteins. Competitive ligand binding studies have also shown CARDIZEM binding is not altered by therapeutic concentrations of digoxin, hydrochlorothiazide, phenylbutazone, propranolol, salicylic acid, or warfarin. Single oral doses of 30 to 120 mg of CARDIZEM result in detectable plasma levels within 30 to 60 minutes and peak plasma levels two to three hours after drug administration. The plasma elimination half-life following single or multiple drug administration is approximately 3.5 hours. Desacetyl diltiazem is also present in the plasma at levels of 10% to 20% of the parent drug and is 25% to 50% as potent a coronary vasodilator as diltiazem. Therapeutic blood levels of CARDIZEM appear to be in the range of 50 to 200 ng/ml. There is a departure from dose-linearity when single doses above 60 mg are given; a 120-mg dose gave blood levels three times that of the 60-mg dose. There is no information about the effect of renal or hepatic impairment on excretion or metabolism of diltiazem.

INDICATIONS AND USAGE

1. **Angina Pectoris Due to Coronary Artery Spasm.** CARDIZEM is indicated in the treatment of angina pectoris due to coronary artery spasm. CARDIZEM has been shown effective in the treatment of spontaneous coronary artery spasm presenting as Prinzmetal's variant angina (resting angina with ST-segment elevation occurring during attacks).
2. **Chronic Stable Angina (Classic Effort-Associated Angina).** CARDIZEM is indicated in the management of chronic stable angina. CARDIZEM has been effective in controlled trials in reducing angina frequency and increasing exercise tolerance.

There are no controlled studies of the effectiveness of the concomitant use of diltiazem and beta-blockers or of the safety of this combination in patients with impaired ventricular function or conduction abnormalities.

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, patients receiving CARDIZEM have exhibited reversible acute hepatic injury as evidenced by moderate to extreme elevations of liver enzymes. (See PRECAUTIONS and ADVERSE REACTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS).

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when CARDIZEM is administered to a nursing woman if the drug's benefits are thought to outweigh its potential risks in this situation.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences, as well as their frequency of presentation, are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%), AV block (1.1%). In addition, the following events were reported infrequently (less than 1%) with the order of presentation corresponding to the relative frequency of occurrence.

Cardiovascular:	Flushing, arrhythmia, hypotension, bradycardia, palpitations, congestive heart failure, syncope.
Nervous System:	Paresthesia, nervousness, somnolence, tremor, insomnia, hallucinations, and amnesia.
Gastrointestinal:	Constipation, dyspepsia, diarrhea, vomiting, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH.
Dermatologic:	Pruritus, petechiae, urticaria, photosensitivity.
Other:	Polyuria, nocturia.

The following additional experiences have been noted:

A patient with Prinzmetal's angina experiencing episodes of vasospastic angina developed periods of transient asymptomatic asystole approximately five hours after receiving a single 60-mg dose of CARDIZEM.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: erythema multiforme; leukopenia; and extreme elevations of alkaline phosphatase, SGOT, SGPT, LDH, and CPK. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg of CARDIZEM have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive measures should be employed in addition to gastric lavage. The following measures may be considered:

Bradycardia	Administer atropine (0.60 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
High-Degree AV Block	Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure	Administer inotropic agents (isoproterenol, dopamine, or dobutamine) and diuretics.
Hypotension	Vasopressors (eg, dopamine or levarterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

The oral/LD_{50}'s in mice and rats range from 415 to 740 mg/kg and from 560 to 810 mg/kg, respectively. The intravenous LD_{50}s in these species were 60 and 38 mg/kg, respectively. The oral LD_{50} in dogs is considered to be in excess of 50 mg/kg, while lethality was seen in monkeys at 360 mg/kg. The toxic dose in man is not known, but blood levels in excess of 800 ng/ml have not been associated with toxicity.

DOSAGE AND ADMINISTRATION

Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm. Dosage must be adjusted to each patient's needs. Starting with 30 mg four times daily, before meals and at bedtime, dosage should be increased gradually (given in divided doses three or four times daily) at one- to two-day intervals until optimum response is obtained. Although individual patients may respond to any dosage level, the average optimum dosage range appears to be 180 to 240 mg/day. There are no available data concerning dosage requirements in patients with impaired renal or hepatic function. If the drug must be used in such patients, titration should be carried out with particular caution.

Concomitant Use With Other Antianginal Agents:

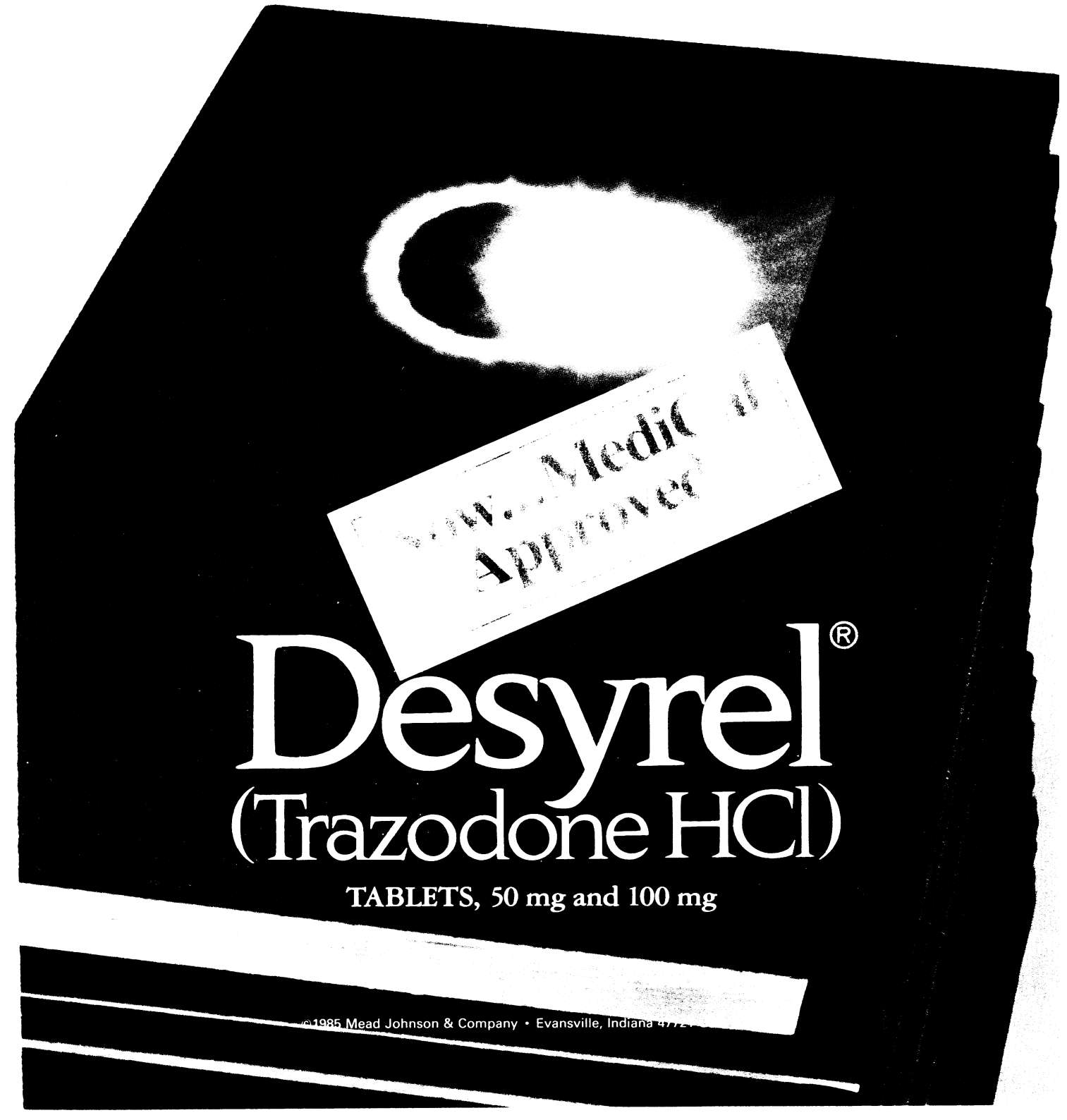
1. **Sublingual NTG** may be taken as required to abort acute anginal attacks during CARDIZEM therapy.
2. **Prophylactic Nitrate Therapy**—CARDIZEM may be safely coadministered with short- and long-acting nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
3. **Beta-blockers.** (See WARNINGS and PRECAUTIONS.)

HOW SUPPLIED

Cardizem 30-mg tablets are supplied in bottles of 100 (NDC 0088-1771-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1771-49). Each green tablet is engraved with MARION on one side and 1771 engraved on the other. CARDIZEM 60-mg scored tablets are supplied in bottles of 100 (NDC 0088-1772-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1772-49). Each yellow tablet is engraved with MARION on one side and 1772 on the other.

Issued 4/1/84

a glowing record



a glowing record of acceptance

Desyrel
(trazodone HCl)

TABLETS 50 mg 100 mg 150 mg

DESCRIPTION
DESYREL® (trazodone hydrochloride) is an antidepressant chemically unrelated to tricyclic, tetracyclic, or other known antidepressant agents. It is a triazolopyridine derivative designated as 2-[3-[4-(3-chlorophenyl)-1-piperazinyl]propyl]-1,2,4-triazolo[4,3-a]pyridin-3-(2H)-one hydrochloride. DESYREL is a white odorless crystalline powder which is freely soluble in water. Its molecular weight is 408.3. The empirical formula is $C_{19}H_{22}ClN_5O \cdot HCl$.

INDICATIONS AND USAGE
DESYREL® (trazodone hydrochloride) is indicated for the treatment of depression. The efficacy of DESYREL has been demonstrated in both inpatient and outpatient settings and for depressed patients with and without prominent anxiety. The depressive illness of patients studied corresponds to the Major Depressive Episode criteria of the American Psychiatric Association's Diagnostic and Statistical Manual, III.[a]

CONTRAINDICATIONS
DESYREL is contraindicated in patients hypersensitive to DESYREL.

WARNINGS
TRAZODONE HAS BEEN ASSOCIATED WITH THE OCCURRENCE OF PRIAPISM. IN APPROXIMATELY 1/3 OF THE CASES REPORTED, SURGICAL INTERVENTION WAS REQUIRED AND, IN A PORTION OF THESE CASES, PERMANENT IMPAIRMENT OF ERECTILE FUNCTION OR IMPOTENCE RESULTED. MALE PATIENTS WITH PROLONGED OR INAPPROPRIATE ERECTIONS SHOULD IMMEDIATELY DISCONTINUE THE DRUG AND CONSULT THEIR PHYSICIAN.

Recent clinical studies in patients with pre-existing cardiac disease indicate that DESYREL may be arrhythmogenic in some patients in that population. Arrhythmias identified include isolated PVCs, ventricular couplets, and in two patients short episodes (3-4 beats) of ventricular tachycardia. Until the results of prospective studies are available, patients with pre-existing cardiac disease should be closely monitored particularly for cardiac arrhythmias. There have also been post-introduction reports of arrhythmias in DESYREL-treated patients, some of whom did not have pre-existing cardiac disease. DESYREL is not recommended for use during the initial recovery phase of myocardial infarction.

PRECAUTIONS
General: The possibility of suicide in seriously depressed patients is inherent in the illness and may persist until significant remission occurs. Therefore, prescriptions should be written for the smallest number of tablets consistent with good patient management. Hypotension, including orthostatic hypotension and syncope, has been reported to occur in patients receiving DESYREL. Concomitant administration of antihypertensive therapy with DESYREL may require a reduction in the dose of the antihypertensive drug. Little is known about the interaction between DESYREL and general anesthetics; therefore, prior to elective surgery, DESYREL should be discontinued for as long as clinically feasible. As with all antidepressants, the use of DESYREL should be based on the consideration of the physician that the expected benefits of therapy outweigh potential risk factors. **Information for Patients:** Alert patients that (a) because priapism has been reported to occur in patients receiving DESYREL, patients with prolonged or inappropriate penile erection should immediately discontinue the drug and consult with the physician; (b) their mental or physical ability to perform potentially hazardous tasks, such as operating machinery or driving, may be impaired; (c) the response to CNS depressants such as alcohol or barbiturates may be enhanced; and (d) DESYREL should be taken shortly after a meal or light snack. **Laboratory Tests:** WBC and differential counts are recommended for patients who develop fever, sore throat or other signs of infection. Discontinue DESYREL if WBC or absolute neutrophil count falls below normal. **Drug Interactions:** Increased serum digoxin or phenytoin levels have been reported to occur in patients receiving DESYREL (trazodone hydrochloride) concurrently with either of those two drugs. Since it is not known whether an interaction will occur between DESYREL and MAO inhibitors, therapy should be initiated cautiously with a gradual increase in dosage until optimum response is achieved, if a MAO inhibitor is discontinued shortly before or is to be given concomitantly with DESYREL. **Therapeutic Interactions:** Concurrent administration with electroshock therapy should be avoided because of the absence of experience in this area. **Carcinogenesis, Mutagenesis, Impairment of Fertility:** No drug- or dose-related occurrence of carcinogenesis was evident in rats receiving DESYREL in daily oral doses up to 300 mg/kg for 18 months. **Pregnancy:** Since there are no adequate and well-controlled studies in pregnant women, DESYREL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nursing Mothers:** Since DESYREL and/or its metabolites have been found in the milk of lactating rats, caution should be exercised when DESYREL is administered to a nursing woman. **Pediatric Use:** Safety and effectiveness in children below the age of 18 have not been established.

ADVERSE REACTIONS
Clinical Trial Reports: Side effects reported by more than 1% of the patients during clinical trials are the following: **Autonomic**—blurred vision, constipation, dry mouth; **Cardiovascular**—hypertension, hypotension, shortness of breath, syncope, tachycardia/palpitations; **CNS**—anger/hostility, confusion, decreased concentration, disorientation, dizziness/light-headedness, drowsiness, excitement, fatigue, headache, insomnia, impaired memory, nervousness; **Gastrointestinal**—abdominal/gastric distress, bad taste in mouth, diarrhea, nausea/vomiting; **Musculoskeletal**—musculoskeletal aches/pains; **Neurological**—incoordination, paresthesia, tremors; **Sexual Function**—decreased libido; **Skin**—allergic condition/edema; and **Other**—decreased appetite, eyes red/tired/itching, head full-heavy, malaise, nasal/sinus congestion, nightmares/vivid dreams, sweating/clamminess, tinnitus, weight gain, weight loss. Side effects reported by less than 1% of the study patients are the following: akathisia, allergic reaction, anemia, chest pain, delayed urine flow, early menses, flatulence, hallucinations/delusions, hematuria, hypersalivation, hypomania, impaired speech, impotence, increased appetite, increased libido, increased urinary frequency, missed periods, muscle twitches, numbness, and retrograde ejaculation. **Post Introduction Reports:** Voluntary reports received since market introduction include the following: agitation, apnea, diplopia, edema, grand mal seizures, hallucinations, hemolytic anemia, liver enzyme alterations, methemoglobinemia, nausea/vomiting (most frequently), paresthesia, priapism (see PRECAUTIONS, Information for Patients; some patients have required surgical intervention), rash, and weakness. Cardiovascular system effects which have been reported are the following: orthostatic hypotension and syncope, palpitations, bradycardia, atrial fibrillation, myocardial infarction, cardiac arrest, arrhythmia, and ventricular ectopic activity, including ventricular tachycardia (see WARNINGS).

OVERDOSE
Signs and Symptoms: Death from overdose has occurred in patients ingesting DESYREL (trazodone hydrochloride) and other drugs concurrently (namely, alcohol; alcohol + chloral hydrate + diazepam; amobarbital; chlordiazepoxide; or meprobamate). The most severe reactions reported to have occurred with overdose of DESYREL alone have been priapism, respiratory arrest, seizures, and EKG changes. The reactions reported most frequently have been drowsiness and vomiting. Overdosage may cause an increase in incidence or severity of any of the reported adverse reactions (see ADVERSE REACTIONS).

DOSAGE AND ADMINISTRATION
The dosage should be initiated at a low level and increased gradually, noting the clinical response and any evidence of intolerance. Occurrence of drowsiness may require the administration of a major portion of the daily dose at bedtime or a reduction of dosage. DESYREL should be taken shortly after a meal or light snack. **Usual Adult Dosage:** An initial dose of 150 mg/day in divided doses is suggested. The dose may be increased by 50 mg/day every three to four days. The maximum dose for outpatients usually should not exceed 400 mg/day in divided doses. Inpatients may be given up to but not in excess of 600 mg/day in divided doses.
Maintenance: Dosage during prolonged maintenance therapy should be kept at the lowest effective level. Once an adequate response has been achieved, dosage may be gradually reduced, with subsequent adjustment depending on therapeutic response.

HOW SUPPLIED
DESYREL® (trazodone hydrochloride) 50 mg and 100 mg scored tablets, and 150 mg DIVIDOSE® tablets.

CAUTION: Federal law prohibits dispensing without a prescription.

REFERENCES
a. Williams JBW, Ed: Diagnostic and statistical manual of mental disorders-III, American Psychiatric Association, May 1980.

U.S. Pat. No. 4,215,104 Date of Latest Revision: July 1985

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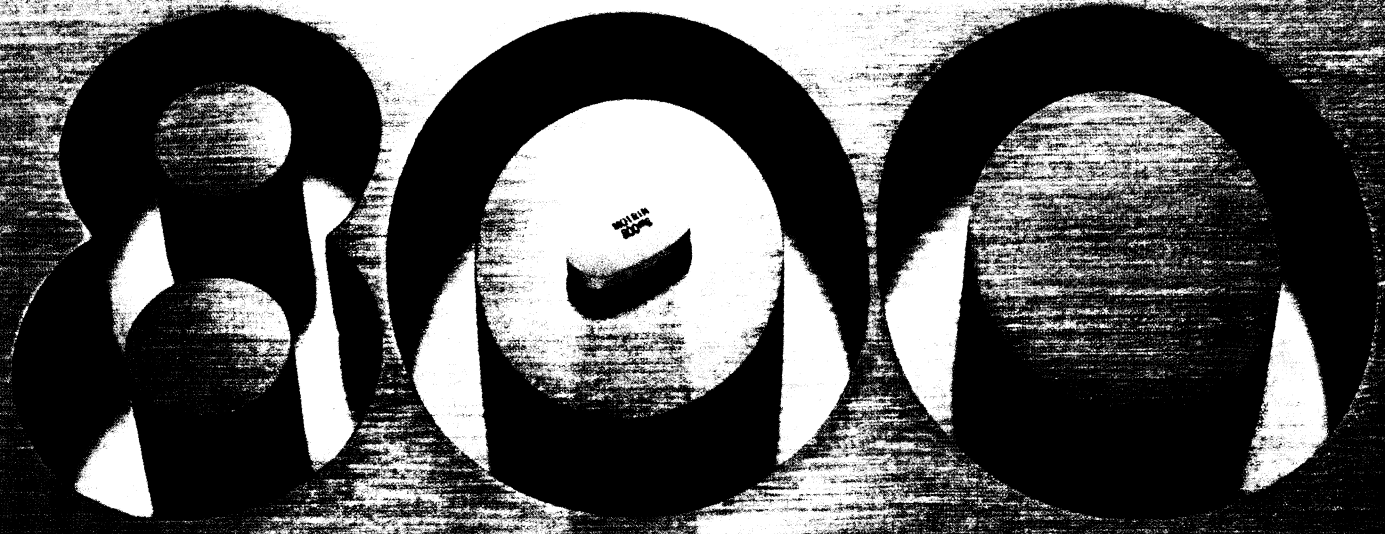

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Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

WARNING

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of Dyrenium (triamterene, SK&F CO.) and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function.

Thiazides may add to or potentiate the action of other antihypertensive drugs.

Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

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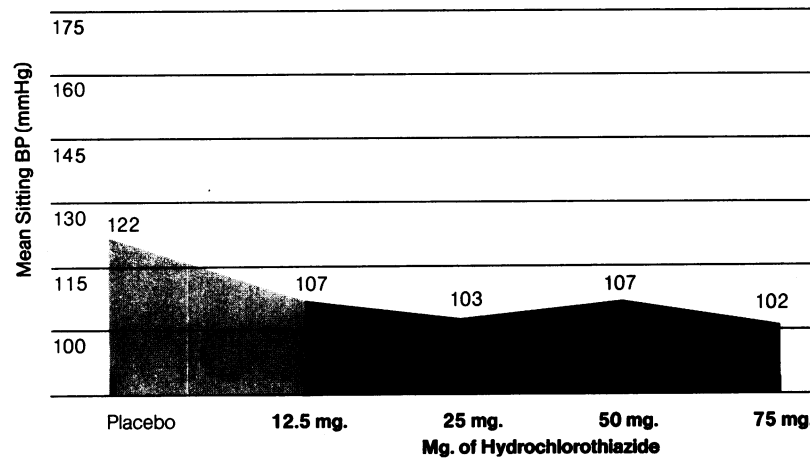

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1. Kaplan, N.: Systemic Hypertension: Therapy, in Braunwald, E. (ed.), Heart Disease. A Textbook of Cardiovascular Medicine, Philadelphia, W.B. Saunders Co., vol. 1, pp. 922-951.

2. Dialogues in Hypertension, Hypertension Update II: New Developments in Antihypertensive Therapy, Jan. 1985, Health Learning Systems Inc.

3. Adapted from Beerman, B., and Groschinsky-Grind, M.: Antihypertensive Effect of Various Doses of Hydrochlorothiazide and Its Relation to the Plasma Level of the Drug, Eur. J. Clin. Pharmacol. 13: 195-201, 1978.

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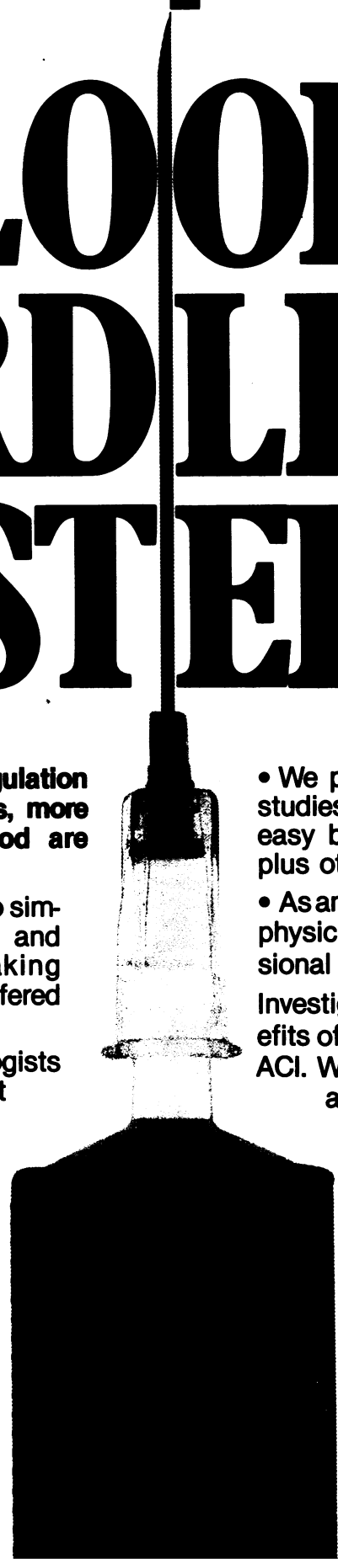

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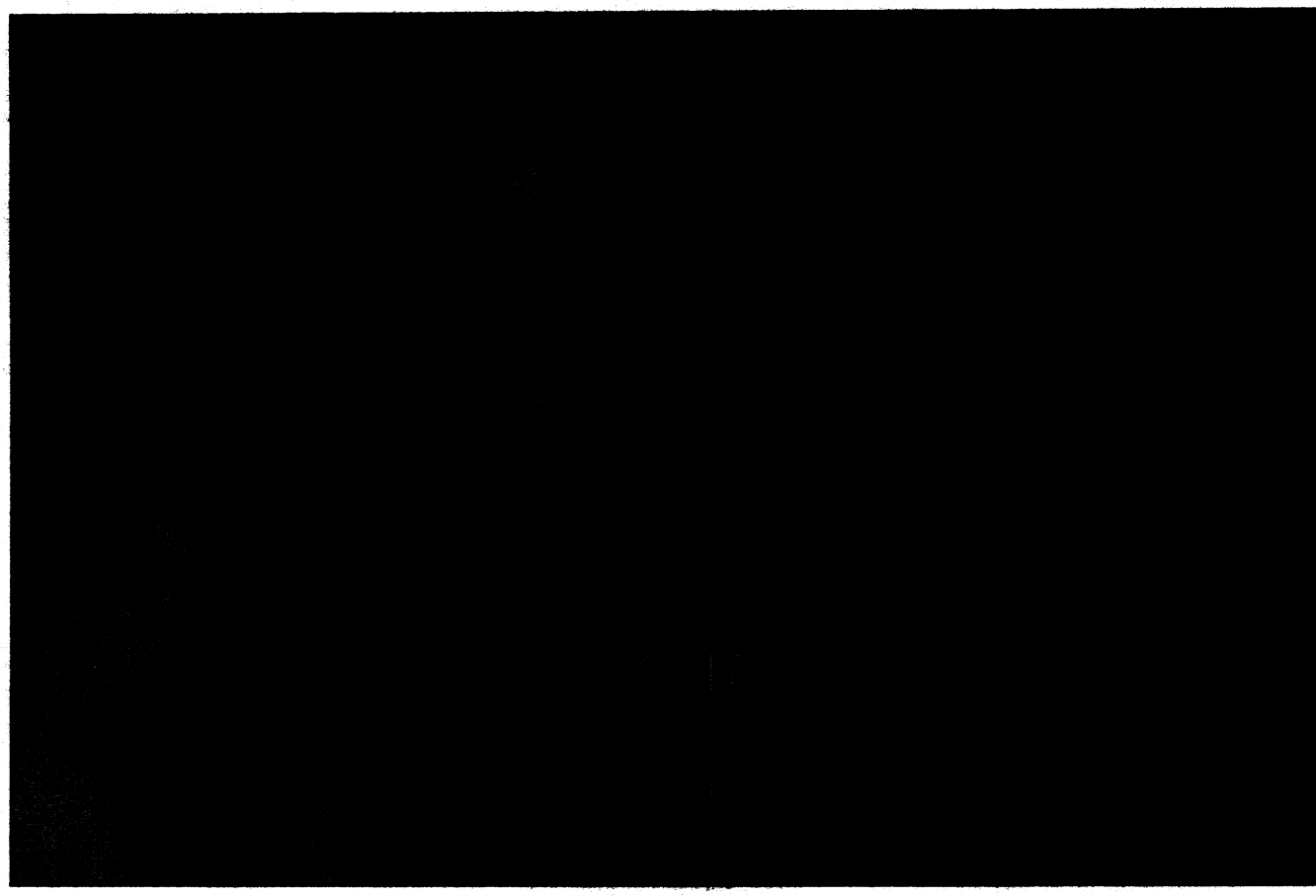

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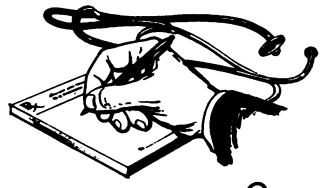

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NEW MEXICO MEDICAL SOCIETY

SCIENTIFIC SESSION: HUMAN SEXUALITY UPDATE—1985

28th INTERIM SESSION

November 14-16, 1985

HOLIDAY INN DE LAS CRUCES
Las Cruces, NM

REGISTRATION

$45, members; after Nov 5—$50
$75, nonmembers; no fee for emeritus, nurses, students
$15, physicians in government service, residents

RESERVATIONS

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201 East University
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(505) 526-4411

November 14, 1985

2:00 PM
COUNCIL MEETING

November 15,1985

8:30 AM
HOUSE OF DELEGATES—
First Meeting

9:15 AM
REFERENCE COMMITTEES

2:00 PM
SCIENTIFIC SESSION—Human Sexuality Update—1985

"The Signs and Symptoms of Sexual Dysfunction"
J. ROBERT MEYNERS, PhD, MASTERS & JOHNSON INSTITUTE

"Age and Sexuality: The Mature/ Postmenopausal Woman"
WALTER G. LEONARD, MD, Boston, Massachusetts

"The Effects of Drugs on Libido"
ALLEN B. ADOLPHE, MD, Albuquerque

"Impotence: Cause and Effect"
ROBERT T. ROSEN, MD

7:00 PM
BANQUET

Speaker: J. R. MEYNERS, PhD
"Effective Treatment of Sexual Dysfunction—The Masters & Johnson Program"

November 16, 1985

9:00 AM
"Psycho-sexual and Psychological Implications of Body Image, Perceived and Real"
BURTON B. WEBER, MD

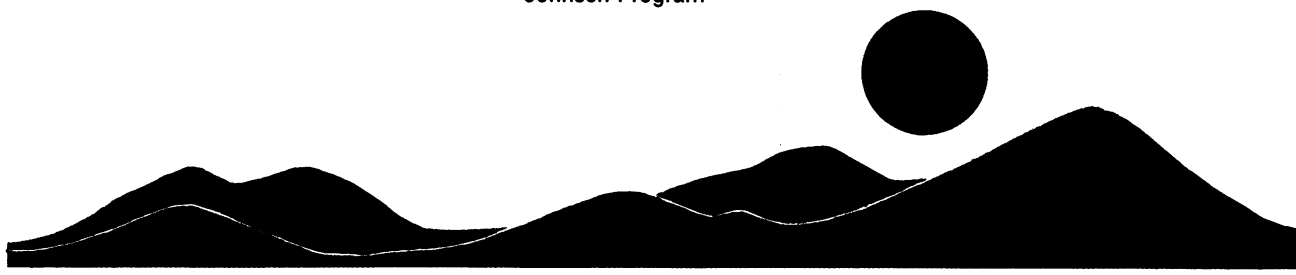
9:40 AM
"Sexual Fulfillment Despite Chronic Disease and Pain"
WALTER G. LEONARD, MD

10:30 AM
SMALL GROUP DISCUSSIONS

11:30 AM
SUMMATION

12:00 NOON
NEMPAC LUNCHEON/SEMINAR—
Political Awareness and Involvement for the Medical Community

2:00 PM
HOUSE OF DELEGATES—
Second Meeting



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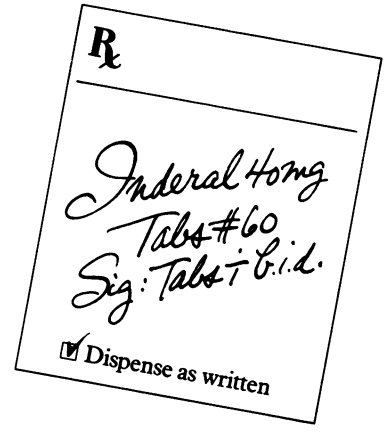
(PROPRANOLOL HCl)

10 mg 20 mg 40 mg 60 mg 80 mg 90 mg*



BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)

INDERAL® (propranolol hydrochloride) Tablets

CONTRAINDICATIONS

INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS

CARDIAC FAILURE: Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)—PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY: The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL, like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA: Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS: Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS

General: Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL (propranolol hydrochloride) may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

Clinical Laboratory Tests: Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS: Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy: Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular: bradycardia; congestive heart failure; intensification of AV block; hypotension; paresthesia of hands; thrombocytopenic purpura; arterial insufficiency, usually of the Raynaud type.

Central Nervous System: Lightheadedness; mental depression manifested by insomnia, lassitude, weakness, fatigue; reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal: nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic: pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory: bronchospasm.

Hematologic: agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune: In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous: alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

*The appearance of INDERAL tablets is a registered trademark of Ayerst Laboratories.

9418/185

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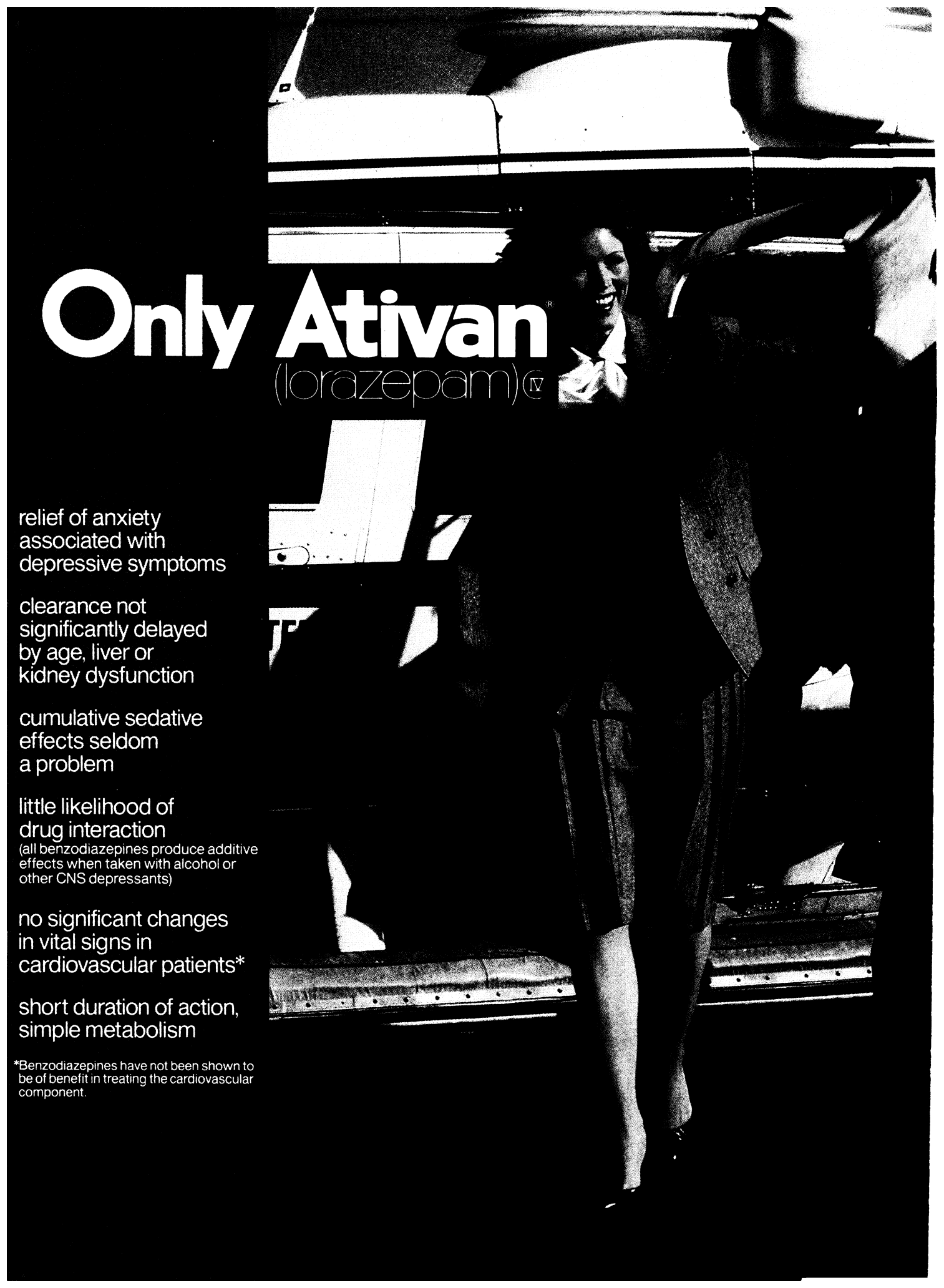

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*Benzodiazepines have not been shown to be of benefit in treating the cardiovascular component.

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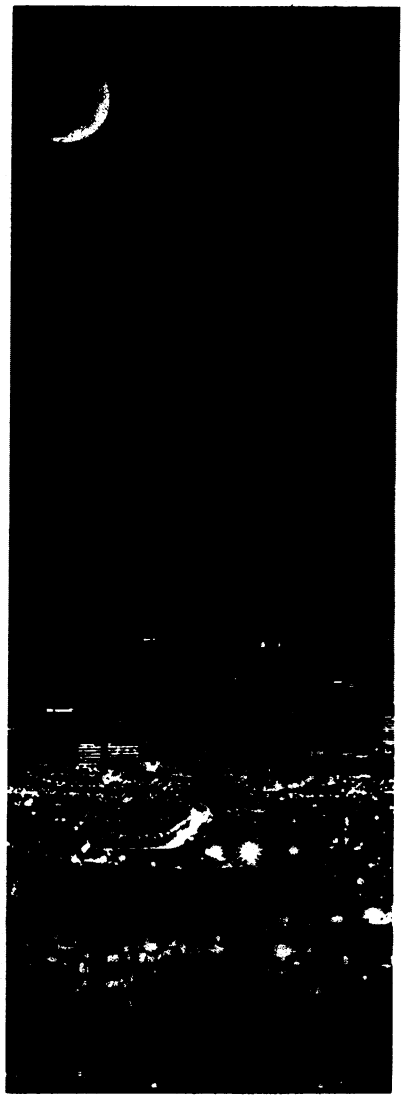
For Brief Summary, please see following page.



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• How coding will input into fee profiles of the future. • Who codes the procedures and diagnoses that you don't! • How the insurance carriers use codes to lower your reimbursement. • Recognition of the diagnosis from the hospital chart or office record. • Use of simplified terminology to relate procedures as they appear "on your records" to the CPT-85. • Defining levels of service for higher reimbursement. • Your patient's chart — how to organize it for ease of coding and office efficiency. • Keys to unlock the complexity of the ICD-9-CM.

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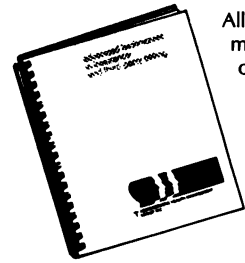
Long Beach	**Oct. 24, 1985**	**Hyatt Edgewater • 6400 E. Pacific Coast Hwy.**
Anaheim	**Oct. 25, 1985**	**Sheraton Anaheim Motel • 1015 W. Ball Rd.**
San Diego	**Nov. 5, 1985**	**Holiday Inn at the Embarcadero • 1355 N. Harbor Dr.**
Torrance	**Nov. 6, 1985**	**Holiday Inn - Torrance • 21333 Hawthorne Blvd.**
Pasadena	**Nov. 7, 1985**	**Holiday Inn of Pasadena • 303 E. Cordova St.**
Las Vegas	**Nov. 8, 1985**	**Flamingo Hilton • 3555 Las Vegas Blvd. S.**
San Francisco	**Nov. 19, 1985**	**Westin St. Francis • 335 Powell St. & Union Square**
Sacramento	**Nov. 20, 1985**	**Holiday Inn - Holidome • 5321 Date Ave.**
Marina Del Rey	**Nov. 21, 1985**	**Marina International Hotel • 4200 Admiralty Way**
Orange County	**Nov. 22, 1985**	**Weston South Coast Plaza • 666 Anton Blvd.**
Palo Alto	**Dec. 2, 1985**	**Hyatt Rickeys • 4219 El Camino Real**
Fresno	**Dec. 3, 1985**	**Ramada Inn • 324 E. Shaw Ave.**
Stockton	**Dec. 4, 1985**	**The Stockton Hilton • 2323 Grand Canal Blvd.**
Los Angeles	**Dec. 5, 1985**	**Hyatt on Sunset • 8401 Sunset Blvd.**
Ventura	**Dec. 6, 1985**	**Holiday Inn on the Beach • 450 E. Harbor Blvd.**

Seminars start at 9 a.m. and are over at 4:30 p.m. each date



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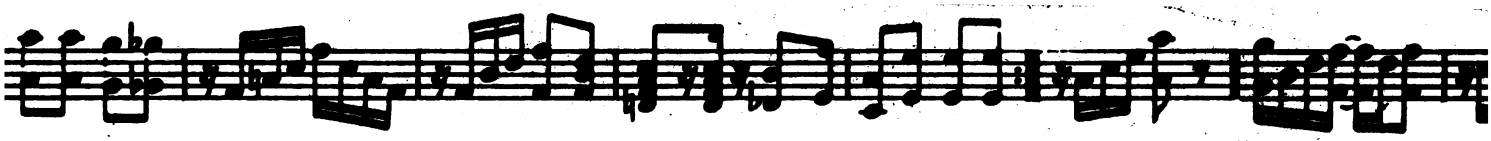

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EMERGENCY PHYSICIAN, San Francisco Bay Area. Leading HMO seeking ABEM certified/residency trained Emergency Physician or Internist with extensive emergency medicine experience for full-time position. Competitive salary with outstanding benefits leading to shareholdership. Send CV to J. A. McCowin, MD, Emergency Dept., Permanente Medical Group, 280 W. MacArthur Blvd., Oakland, CA 94611, or call (415) 428-5634.

URGENT CARE CLINIC: Vacaville, CA. Full time family practice oriented emergency physician. Twelve hours/day. Guarantee plus percentage. Malpractice provided. Minimum one year commitment. Please reply to Kendall R. Bauer, MD, PO Box 860, Folsom, CA 95630. For information about this position call (916) 933-1449 (evenings).

CALIFORNIA, NORTHERN: We are seeking career-oriented emergency physicians to staff the emergency department at the new Kaiser Hospital in South Sacramento. Advantages include ideal location midway between San Francisco and the Sierra Nevada Mountains, excellent patient mix, freedom from contract billing hassles, competitive salary, and outstanding fringe benefits. Send CV to William Durston, MD, c/o Mrs. Carolyn Whelan, The Permanente Medical Group, Inc., PO Box 254999, Sacramento, CA 95825. An equal opportunity employer.

FAMILY PRACTITIONER—position available with 35-member multispecialty group; BC/BE; immediate opening; full range of benefits plus early shareholding status; excellent opportunity; central coast of California. Submit CV to Colin J. Wells, MD, San Luis Medical Clinic, Ltd., 1235 Osos St., San Luis Obispo, CA 93401.

PHYSICIANS WANTED

CALIFORNIA, SONOMA COUNTY—B/C or B/E FP to associate with B/C FP in growing community 60 minutes north of San Francisco. Salary or percentage to start. Hours negotiable. Contact Thomas H. Moore, DO; (707) 795-4560.

PSYCHIATRIST—Board eligible, half-time salaried inpatient position with county/private patients. Private practice inpatient/outpatient available. Bilingual in Spanish preferred. Apply to Owen Lum, MD, Dominican Santa Cruz Hospital Mental Health Unit, 1555 Soquel Dr., Santa Cruz, CA 95060; or call (408) 476-0220, Ext. 1400.

PULMONOLOGIST, Boarded Internal Medicine and Board eligible Pulmonology, to join 35-member multispecialty group located on the California central coast. Premium location, excellent practice opportunity with fully paid benefit and retirement program; guaranteed salary first six months followed by incentive pay program; all practice costs paid. For more information contact: Colin Wells, MD, Recruitment Coordinator, or David Graham, Associate Administrator, San Luis Medical Clinic, Ltd., 1235 Osos St., San Luis Obispo, CA 93401; (805) 546-5600.

TWO FULL-TIME FACULTY POSITIONS available in the Department of Family Practice, University of California, Davis; level of appointment commensurate with academic experience and credentials. Should be Board certified by the American Board of Family Practice with interest, training, and/or experience in teaching, research and academic publication activities. These positions will remain open until filled . . . applications will not be accepted after 12/31/85. Send CV to Robert C. Davidson, MD, Chair, Department of Family Practice, University of California, Davis, 2221 Stockton Blvd., Sacramento, CA 95817. The University of California is an affirmative action, equal opportunity employer.

PEDIATRICIAN: Immediate opening for Board eligible/certified Pediatrician with the Western Montana Clinic in an outstanding university town of 30,000 with excellent practice, recreational, and educational opportunities. Contact: Wesley W. Wilson, MD, Western Montana Clinic, 515 West Front St., Missoula, MT 59802.

SANTA BARBARA, CA—Internist, Board certified/eligible, energetic General Internist to join well-established group of rehabilitation physicians in beautiful coastal city to provide internal medicine care for 46 bed freestanding hospital specializing in treatment of physical disabilities, e.g., strokes, spinal cord injuries, traumatic head injuries, amputees. Salary negotiable. Contact: Martin Wice, MD, Box 3098, Santa Barbara, CA 93130.

PHYSICIANS WANTED

WESTERN WASHINGTON—Private practice openings in Family Practice, Internal Medicine, Pulmonary, OB/GYN, and Otolaryngology. For information, please call Eloise Gusman, 1 (800) 535-7698; or send CV to 2800 Veterans Blvd., Suite 170, Metairie, LA 70002.

FACULTY MEMBER OF COMP looking for associate interested in structural rehabilitation. Opportunity to build an exciting practice at a large preventive medical clinic with DOs and MDs in beautiful La Jolla, California. Opening immediately. For information, contact Ruth I. Gotsch, DO, 8950 Villa La Jolla Dr., Suite 2162, La Jolla, CA 92037; (619) 457-1314.

IM/FP—American trained BC/E Internist and BC/E Family Practitioner needed by growing group practice. Salary plus benefits first year. Partnership plus incentive second year. Longevity a must. Spanish speaking helpful. South and East of downtown Los Angeles. Send CV to Medical Director, Box 6495, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

FAMILY PRACTICE-INTERNAL MEDICINE-SURGEON. Multispecialty clinic in Northern Idaho Panhandle. Nominal lease includes fully-equipped office and treatment suites with receptionist and janitorial services provided. Clinic includes x-ray, lab and pharmacy. Billing services available. Located in a four-season playground rich with recreational opportunities. Just 20 minutes from a 14-run ski resort. For information: (208) 784-1221, X304. Mail résumés to: Shoshone Medical Center, Jacobs Gulch, Kellogg, ID 83837.

INTERNIST with sub-speciality to join six established in Mountain View, California. Near 450 bed, well equipped hospital and Stanford University. Send CV to El Camino Internal Medical Group, Inc., 125 South Dr., Mountain View, CA 94040.

OPPORTUNITY IN THE SCENIC PACIFIC NORTHWEST. Position: BE or BC FP needed to join three Family Practitioners in established North Seattle Group as replacement for fourth associate. Our practice includes obstetrics. Send CV to L. Lippman, MD, 18514 Firlands Way North, Seattle, WA 98133.

SAN DIEGO—Orthopedist needed for practice specializing in Worker's Compensation. Excellent salary; possible partnership. Call Frances (619) 296-6226.

THE UNIVERSITY OF UTAH, Department of Family and Community Medicine, is seeking two BC/BE Family Physicians for clinical positions in university-run community health centers. The population served is a challenging, multi-ethnic one. Full range of family practice including obstetrics, is required. Flexibility exists for resident teaching, research, and post-graduate work towards MSPH. Attractive base salary, benefits, practice incentive, and vacation time. If interested call or write Dr Stephen Ratcliffe, University of Utah, DFCM, 50 North Medical Dr., Salt Lake City, UT 84132; (801) 581-5529.

KETCHUM, SUN VALLEY, IDAHO: Internist, OB/GYN, Pediatrician, Orthopedist in multispecialty, expanding, well-equipped clinic. Income moderate; quality of life highest. Dr Bryan Stone, PO Box 2198, Ketchum, ID 83340; (208) 726-9361.

WALLA WALLA CLINIC is accepting applications for BC/BE second Gastroenterologist to join a busy GI service. Walla Walla Clinic is a 30 physician multispecialty clinic serving an immediate county of 60,000 with a referral population of 150,000 people. Walla Walla is a sophisticated regional medical center with most medical and surgical subspecialties, outstanding technological support (CT scanning, digital angiography, nuclear medicine, ultrasonography). Walla Walla offers excellent cultural, recreational, and educational facilities. Climate is mild and life-style relaxed. Guaranteed salary and immediate full participation in the incentive program. Outstanding benefit package. Please submit your CV to Lawrence S. Zawatzky, MD or to Search Committee, Walla Walla Clinic, 55 West Tietan, Walla Walla, WA 99362.

PHYSICIANS WANTED

WANTED—FAMILY PRACTICE ASSOCIATE— Pleasant Central California community close to mountains, ocean, San Francisco and Los Angeles. Medical school affiliation possible. Well established general practice with light obstetrics. Salary plus incentive. Available immediately. Woman preferred. Reply to Kathleen A. Baron, MD, 1163 East Warner Ave., Fresno, CA 93710; (209) 432-1700.

WASHINGTON COASTAL COMMUNITY serving a population of 65,000 is actively recruiting the following specialists: Orthopedic Surgeon, Urologist, Otolaryngologist, General Surgeon. A variety of practice support options are available, i.e. office space, relocation assistance, etc. Enjoy the support of major West Coast Catholic Hospital System. Community has close proximity to major recreational areas and easy access to Seattle and Portland. For information send CV and references to: Nancy Friedrich, The Friedrich Group, 9284 Ferncliff N.E., Bainbridge Island, WA 98110.

CALIFORNIA: University of California Davis Medical Center, Division of Emergency Medicine. Full-time positions are available for physicians in the Division of Emergency Medicine. We are an academic medical center and the trauma center for a large region of Northern California. The positions are clinical faculty appointments with the University of California Davis School of Medicine and entail direct patient care in the Emergency Department as well as teaching the housestaff and medical students of the University of California Davis Medical Center. Applicants should send curriculum vitae to Robert Derlet, MD, Division of Emergency Medicine, UCDMC, 2315 Stockton Blvd., Trailer 1219, Sacramento, Ca 95817.

FAMILY PRACTITIONER—Full-time position available for residency trained, Board eligible/Board certified Family Practitioners interested in practicing in a comprehensive care environment. Outpatient care and in-hospital responsibilities are offered in a growing family practice organization. Administrative opportunities also available. For information, call William Trainor, Manager Professional Staffing, toll-free 1 (800) 446-2255; in California call 1 (800) 336-2255. FHP Professional Staffing, 400 Oceangate Blvd., Suite 1317, Long Beach, CA 90802. For opportunities in Utah, call Maryalys Poulson, collect, at (801) 355-1234.

CAREER OPPORTUNITY for Family Physician with well established group of six in Southern California. Full partnership available after trial period. Beautiful family type community in San Diego County. Résumé to Box 6496, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

THORACIC VASCULAR GENERAL SURGEON—To associate with senior Surgeon. Well established referral practice. Salary plus percentage. Central California. Send curriculum vitae to Box 7001, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

PHYSICIANS WANTED

PHYSICIAN, Board certified or eligible in Occupational Medicine, wanted for Los Angeles company of 10,500. Excellent benefits, stable employment for qualified person. California license required. Call Medical Director, (213) 481-4969, or write Medical Director, PO Box 111, Los Angeles, CA 90051.

FACULTY POSITION AVAILABLE: Eighteen-resident fully accredited program affiliated with University of Washington. City of 105,000 with multiple cultural and recreational opportunities. Excellent salary and benefits. Board certified in Family Practice required. Send CV to John Mohr, MD, Director, 777 N. Raymond, Boise, ID 83704.

INTERNIST wanted to join five-man Board certified internal medicine group. Desirable San Francisco Bay Area community. Please reply Box 7000, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

SEATTLE EMERGENCY ROOM: Full-time position in moderate volume hospital. Prefer internal medicine with background in critical care or emergency. Reply: Recruiter, 1221 Madison #315, Seattle, WA 98104.

PRIMARY CARE PHYSICIANS needed in Seattle Suburban Community now. In response to community needs, a major full-service hospital is encouraging the development of Primary Care Physician Practices. Commercial financing contracts are being arranged by the hospital. This high-growth, high-employment community has some existing practices available. For more information, please call or write The Friedrich Group, 9284 Ferncliff N.E., Bainbridge Island, WA 98110; (206) 842-5248 or (206) 329-0417.

OBSTETRICIAN-GYNECOLOGIST—Personable and industrious female Obstetrician-Gynecologist desired to join 3-physician department in 28-physician multispecialty group. Immediate practice opportunity. Drawing area 185,000. Western slope of the Rockies. Excellent hospital facilities. Superb living conditions. Unexcelled skiing and outdoor recreation. Primary fee-for-service. HMO option. Please send curriculum vitae and references to Mary Beard, MD, Ogden Clinic, 4650 Harrison, Ogden, UT 84403.

MEDICAL DIRECTOR—Family Health Foundation of Alviso offers challenging opportunity to systems oriented physician for Prepaid Health Plan and fee for service health center. Excellent salary. Req: California Medical License; one year of formal training in health administration or two years experience in medical care management and proficiency in primary clinical care. Please submit résumé to James M. Clayton, CEO, FHFA, 1621 Gold St., Alviso, CA 95002. EOE.

LARGE, WELL ESTABLISHED Internal Medicine group seeking General Internist to join its practice leading to partnership. Excellent suburban San Diego location. Send CV to Frank Millward, PO Box 9001, La Mesa, CA 92041-9001.

PHYSICIANS WANTED

ROSEVILLE (PLACER COUNTY): The Oakridge Medical Clinic, a seven physician Family Practice Group has an opening for a Board eligible or certified Family Practitioner. Salary initially with anticipated buy-in later. No initial investment. Large medical facility with x-ray, lab, and minor surgery. Excellent location situated next to a 250 bed community hospital. No OB. On call every seventh weekend, four day work week, seven weeks vacation per year. Excellent fringe benefits. Beautiful, rapidly growing Northern California Sierra Foothill Community near Sacramento. Unlimited surrounding recreational facilities. Contact: William A. Anthony, Jr, MD, Roseville, CA 95678; (916) 782-1221.

SANTA BARBARA COUNTY: You're needed in Northern Santa Barbara County! Santa Barbara County Health Care Services has full-time salaried positions available for BC/BE Family Practitioners interested in a position involving primary outpatient care in our Santa Maria clinic. We offer a unique opportunity to practice quality medicine in a multispecialty community clinic. Shared call with four other primary care physicians. Close to Central California's spectacular coastline as well as other inland recreational areas. Knowledge of Spanish helpful but not required. Send CV to: Gary Erbeck, MPH, Santa Barbara County Health Care Services, 300 San Antonio Rd., Santa Barbara, CA 93110.

HAWAII, GARDEN ISLAND OF KAUAI: Internal Medicine physician with preferable extra training and/or experience in pulmonary medicine and/or allergic disorders. Practice on the beautiful island of Kauai with 35-member hospital-based multispecialty group. Call or write to: Neal Sutherland, MD, Kauai Medical Group, 3420-B Kuhio Highway, Lihue, HI 96766. Phone: (808) 245-1554.

GASTROENTEROLOGIST FOR LOS ANGELES AREA—Association leading to partnership with established physician. For details, call Eloise Gusman, 1 (800) 535-7698; or send CV to 2800 Veterans Blvd., Suite 170, Metairie, LA 70002.

PHYSICIAN WANTED—California, Fresno area. Two Board certified Family Practitioners seeking third associate. Practice opportunities include, Surgery, ER, and OB if desired. Send CV to PO Box 922, Selma, CA 93662 or call (209) 896-2624.

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A State Application (Form 678) must be received between October 28, 1985 and November 25, 1985. Any postmarked after that date will not be accepted. All applications will be screened and only those qualified will be accepted to participate in the oral examination. Send a State Application to: Department of Consumer Affairs, Examination Unit, 1020 N Street, Room 535, Sacramento, CA 95825. (916) 324-6513.

(Continued on Page 572)

PHYSICIANS

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(Continued from Page 570)

PHYSICIANS WANTED

SAN JOAQUIN VALLEY: Sports medicine opportunity for an Emergency Physician in an acute injury center and sports medicine clinic will train for orthopedic assisting. No nights. Salary range $88-98,000 includes malpractice plus production bonus. Average 40 hours/week. Contact Star Injury Center and Sports Medical Clinic, 6143 N. Fresno, Ste 108, Fresno, CA 93710.

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Prestigious HMO is seeking experienced specialists and general practitioners for our facilities in Los Angeles and Orange Counties. Located in close proximity to major teaching centers, we offer the opportunity for continued professional development and rewarding clinical practice. Excellent compensation and benefits including paid malpractice, life, disability, medical and dental coverage, paid vacations, sick leave, educational leave and retirement plan. Please send CV to: Director/Physician Recruitment, CIGNA Healthplans of California, 700 North Brand Blvd., Suite 500-49, Glendale, CA 91203.

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At Westworld Community Healthcare, Inc., physicians have something very special: **Time.** Time to devote to their practices, and to their patients. And they have the time because we handle all the business details their practices demand.

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PRACTICE WANTED

PATHOLOGY PRACTICE with clinical genetic toxicology research sought by pathology resident (AP/CP) finishing early-mid 1986, taking pathology boards Spring 1986. Seek concurrent conventional pathology responsibilities and chance to monitor human mutagen exposure. California, Wisconsin licenses. PhD in Biophysics. Extensive experience in animal cell culture and mutagenesis assays. References and curriculum vitae available. Particular interest in Northern California practice; will also consider other locations. Write Dr Busch, Dept. of Pathology, University of Wisconsin Hospital and Clinics, 600 Highland Ave., Madison, WI 53792.

PRACTICES AVAILABLE

ORTHOPAEDIC PRACTICE—Orange County, California, adjacent to major hospital; five additional hospitals in 5-mile radius; will aid in transition. Box 4191, Irvine, CA 92714.

CALIFORNIA: Urology, Surgery, Allergy, Orthopedics, Pediatrics, Internal, Family, OB-GYN, Otolaryngology, others. Contact Mary Bradshaw, Practice Broker/Recruiter, 21 Altamount Dr., Orinda, CA 94563, (415) 376-0762.

IMMEDIATE OPENING for Urologist to take over long established practice in California. Doctor retiring because of illness. For further information call (805) 327-3569.

FAMILY PRACTICE. Well established Coastal Monterey County, California. Retiring. Practice and building for sale. Reasonable price with negotiable terms. Available now. Call (408) 375-2393 or write 48 Castro Rd., Monterey, CA 93940.

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SAN LEANDRO: Prime, central. Prestige medical building. Ample parking. *Great* opportunity Internist or GP. Carol Bull, (415) 357-8940.

FOR SALE: Well designed Medical Clinic in Northern Idaho town. 7,200 square feet, full x-ray department, full laboratory department. Four doctor capacity. Contact Mark Jackson, Attorney; 1 (208) 667-0637.

SITUATIONS WANTED

PATHOLOGIST—Board certified AP, CP. Twelve years experience. Strong background Surgical Pathology with special interests Hematopathology and Cytopathology. Seeks position as associate in preferably group practice. Western states preferred. Available immediately. B. Swinyer, MD, 7805 Buena Tierra, Bakersfield, CA 93309.

SERVICES

PATIENT NEWSLETTER: Keeping in touch shows that you care! Send for your free sample copy of our quarterly health promotion newsletter. Customized for you. Mailing service option. Rx: Live well, 6809 Santa Maria Ln., Dallas, TX 75214-2847 or call (214) 821-5218.

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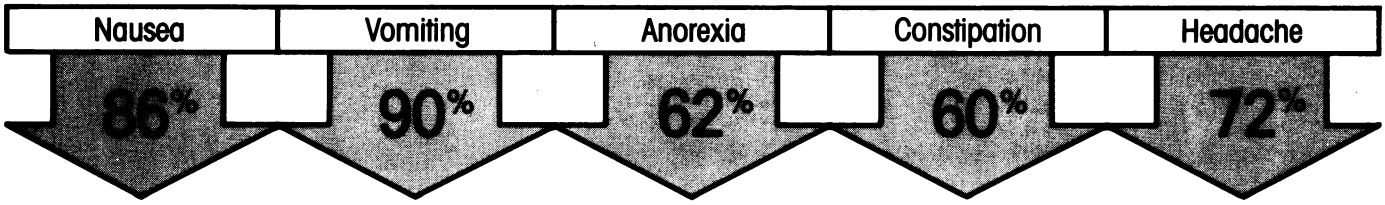
FIRST WEEK—OTHER SOMATIC SYMPTOMS MARKEDLY REDUCED[1]



FOURTH WEEK—PATIENT COMPLIANCE WAS BETTER[2]

More than three times as many amitriptyline patients as Limbitrol patients dropped out of therapy because of side effects, although the incidence of side effects was similar. Caution patients against the combined effects of Limbitrol with alcohol or other CNS depressants and about activities requiring complete mental alertness, such as operating machinery or driving a car. In general, limit dosage to lowest effective amount in elderly patients.

References: **1.** Data on file, Hoffmann-La Roche Inc., Nutley, NJ. **2.** Feighner JP, *et al: Psychopharmacology 61*:217-225, Mar 22, 1979.

Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) Ⓒ Ⓥ

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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of moderate to severe depression associated with moderate to severe anxiety.

Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use; then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.

Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma. Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs. Closely supervise cardiovascular patients. (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving).

Usage in Pregnancy: **Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage; withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).

Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. When tricyclic antidepressants are used concomitantly with cimetidine (Tagamet), clinically significant effects have been reported involving delayed elimination and increasing steady state concentrations of the tricyclic drugs. Concomitant use of Limbitrol with other psychotropic drugs has not been evaluated; sedative effects may be additive. Discontinue several days before surgery. Limit concomitant administration of ECT to essential treatment. See Warnings for precautions about pregnancy. Limbitrol should not be taken during the nursing period. Not recommended in children under 12. In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects.

Adverse Reactions: Most frequently reported are those associated with either component alone: drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion. Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.

The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs:

Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke.

Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido.

Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns.

Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract.

Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus.

Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia.

Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue.

Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female, elevation and lowering of blood sugar levels, and syndrome of inappropriate ADH (antidiuretic hormone) secretion.

Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.

Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. I.V. administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment.

Dosage: Individualize according to symptom severity and patient response. Reduce to smallest effective dosage when satisfactory response is obtained. Larger portion of daily dose may be taken at bedtime. Single *h.s.* dose may suffice for some patients. Lower dosages are recommended for the elderly.

Limbitrol DS (double strength) Tablets, initial dosage of three or four tablets daily in divided doses, increased up to six tablets or decreased to two tablets daily as required. Limbitrol Tablets, initial dosage of three or four tablets daily in divided doses, for patients who do not tolerate higher doses.

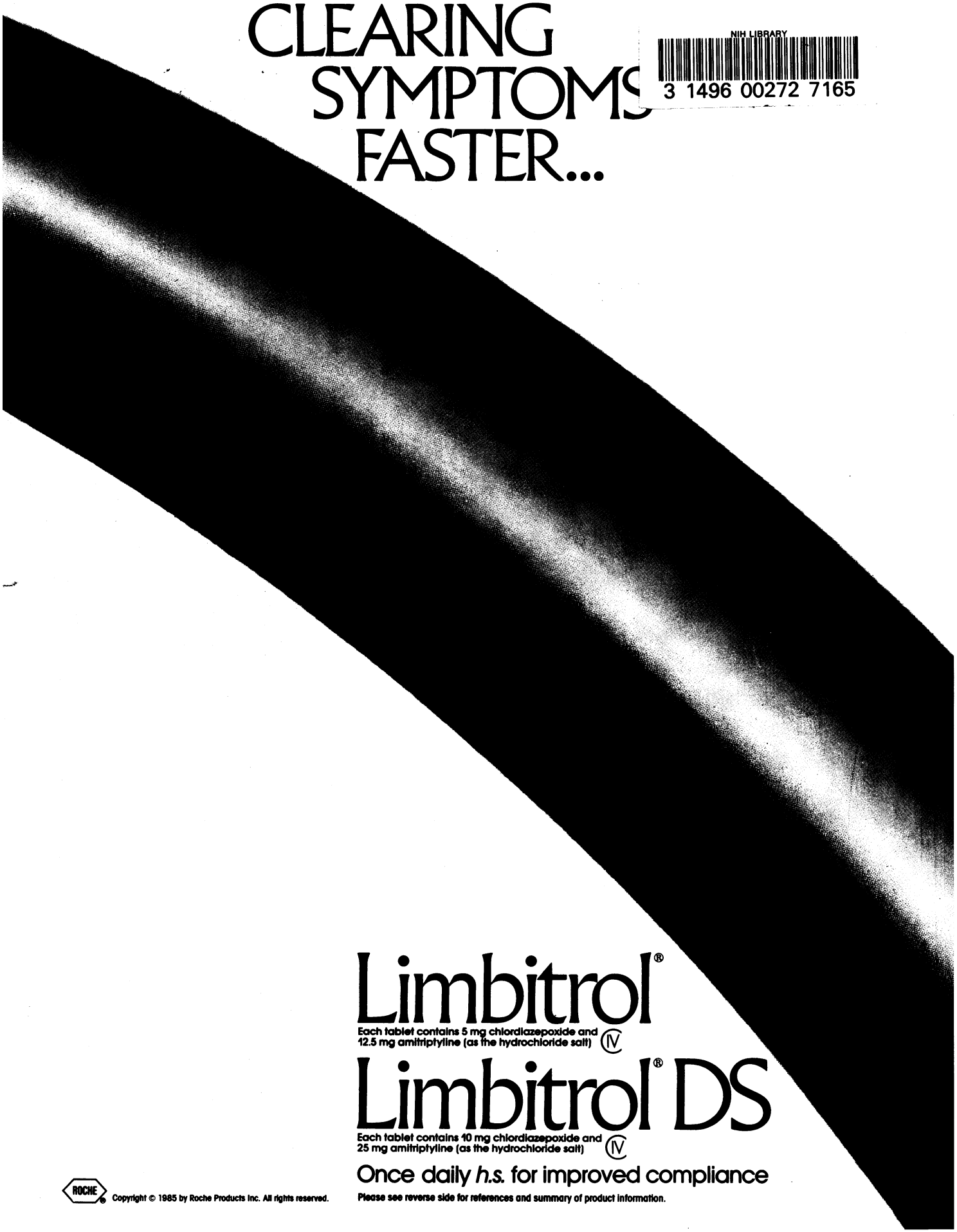
How Supplied: *Double strength (DS) Tablets*, white, film-coated, each containing 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt), and *Tablets*, blue, film-coated, each containing 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt). Available in bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 50.

ROCHE

ROCHE PRODUCTS INC.
Manati, Puerto Rico 00701

In depression and anxiety

CLEARING SYMPTOMS FASTER...



Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) Ⓒ

Limbitrol® DS

Each tablet contains 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) Ⓒ

Once daily *h.s.* for improved compliance

ROCHE

Please see reverse side for references and summary of product information.